# SPECT Imaging of the Brain:
## Comparison of Findings in Patients with Chronic Fatigue Syndrome, AIDS Dementia Complex, and Major Unipolar Depression

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**OBJECTIVE. Chronic fatigue syndrome is an illness of unknown origin that begins abruptly with a flulike state and has symptoms suggesting both a chronic viral encephalitis and an affective disorder. We compared single-photon emission computed tomography (SPECT) scans of patients with chronic fatigue syndrome with those of patients with AIDS dementia complex and unipolar depression.**

**SUBJECTS AND METHODS. We used $^{99m}$Tc–hexamethylpropyleneamine oxime to examine 45 patients with chronic fatigue syndrome, 27 patients with AIDS dementia complex, and 14 patients with major unipolar depression. Scans of 38 healthy persons were used as controls. Comparison of regional defects between groups, as well as midcerebral uptake indexes (an objective measure of global radionuclide uptake), was performed by using analysis of variance with the Student-Newman-Keuls option. Correlation between the number of regional defects and the midcerebral uptake index was determined by using the Spearman rank-correlation test.**

**RESULTS. Patients with AIDS dementia complex had the largest number of defects (9.15 per patient) and healthy patients had the fewest defects (1.66 per patient). Patients with chronic fatigue syndrome and depression had similar numbers of defects per patient (6.53 and 6.43, respectively). In all groups, defects were located predominantly in the frontal and temporal lobes. The midcerebral uptake index was found to be significantly lower ($p < .002$) in the patients with chronic fatigue syndrome (.667) and patients with AIDS dementia complex (.650) than in patients with major depression (.731) or healthy control subjects (.716). Also, a significant negative correlation was found between the number of defects and midcerebral uptake index in patients with chronic fatigue syndrome and AIDS dementia complex, but not in depressed patients or control subjects.**

**CONCLUSION. These findings are consistent with the hypothesis that chronic fatigue syndrome may be due to a chronic viral encephalitis; clinical similarities between chronic fatigue syndrome and depression may be due to a similar distribution and number of defects in the two disorders.**

*AJR* 1994;162:943–951

Chronic fatigue syndrome (CFS) is a condition characterized by varying degrees of chronic fatigue and persistent or recurring fever, pharyngitis, myalgia, headache, arthralgia, paresthesias, depression, and difficulty with concentration and memory [1, 2]. Typically, the chronic illness begins abruptly with an acute flulike syndrome, from which the patient appears to have never fully recovered. The patient's medical history generally is unremarkable except for a three- to fourfold increased frequency, compared with the general population, of both atopic and allergic illnesses [3]; there may [4] or may not [5] also be an increased frequency of past episodes of major depression. Case definitions for the syndrome have been developed by the United States Centers for Disease Control (CDC) [1] and by British [6] and Australian [7] investigators. By definition, in patients with CFS there is no evidence of rheumatologic, endocrinologic, infectious, malignant, or other chronic diseases, and no active psychiatric disease at the onset of the syndrome.

Received August 4, 1993; accepted after revision December 14, 1993.

Supported by grants R01AI27314, R01AI26788, and U01AI32246 from the National Institute of Allergy and Infectious Diseases.

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0361–803X/94/1624–0943

The origin of CFS is unknown and controversial. Clinicians appear to be divided as to the nature of the illness. At one extreme of opinion are those who believe the illness is a purely physical condition, most likely due to infection with a novel infectious agent. At the other extreme are those who believe that all the symptoms of the illness are due to an unrecognized and untreated underlying primary psychiatric disorder, most likely a form of unipolar depression. In all likelihood, CFS, like most illnesses, has both organic and psychiatric components. Although some of the symptoms of CFS, such as the sudden onset, recurrent fevers, adenopathy, and night sweats, suggest an infectious origin, others, such as headaches, sleep disturbance, and difficulty with concentration, are also common in depression and generalized anxiety disorder.

At present, the diagnosis of CFS is made predominantly on clinical grounds, although serologic and immunologic correlates of the disease continue to be investigated. Unfortunately, because the symptoms of CFS are subjective and nonspecific, the disease is likely to be misdiagnosed. Previously, we studied the MR findings in an outbreak of CFS [8]. In the preceding article in this issue of *AJR*, we report that patients with CFS tend to have more abnormalities shown by single-photon emission computed tomography (SPECT) than control subjects do and that SPECT is more sensitive than MR for identifying CNS abnormalities [9]. In this article, we explore the specificity of SPECT for distinguishing patients with CFS from patients with a viral encephalitis (early AIDS dementia complex [ADC]) and from patients with unipolar major depression.

## Subjects and Methods

### *Selection of Subjects*

*Patients with CFS.*—From a group of 360 patients with suspected CFS seen by one of us, 251 patients fully met the CDC, British, or Australian case definitions for CFS [1, 6, 7]. Of these 251, 45 were studied with SPECT between 1991 and 1992. The mean age of the group was 43.3 ± 11.06 (±SD); 64% were female. Among these 45 patients, 10 had a history of an acute CNS event, consisting of seizures, transient visual impairment, or temporary weakness. Thirty-five had more chronic, possibly neurologic symptoms, which included photophobia, paresthesias, and disequilibrium. Sixteen of these patients were reported in the preceding article [9].

*Patients with ADC.*—Twenty-seven patients met the American Academy of Neurology criteria for ADC, or HIV-1–associated cognitive/motor complex (HIV encephalopathy) [10]. SPECT results in some of these patients have been reported [11]. Each had antibodies to HIV and CD4+, T-cell counts below 500/$mm^3$, and cognitive impairment and/or focal neurologic signs without evidence of another infectious or neoplastic process in the CNS. The mean age of the group was 39.6 ± 8.6 years; 11% were female.

*Patients with unipolar depression.*—A group of 14 patients, all of whom met explicit criteria for major depressive disorder, unipolar, as set forth in the *Diagnostic and Statistical Manual of Mental Disorders* (DSM–IIIR) developed by the American Psychiatric Association [12], was recruited from a general adult psychiatric service. The diagnosis was established through a psychiatric interview conducted by a psychiatrist, after patients had been referred by their attending psychiatrist. Patients were excluded from the study if evidence of neurologic disease, severe medical illness, dementia, or a history of head injury or alcoholism was noted. The majority of patients were on antidepressant medication at the time of the SPECT examination, but had not yet exhibited remission of the depressive symptoms. The mean age of the group was 70.0 ± 13.2 years; 64% were female.

*Healthy control subjects.*—Thirty-eight persons who explicitly denied any chronic illness, and who described themselves as in good health, volunteered to undergo SPECT scanning in response to solicitations. Most were spouses of patients being scanned for other reasons, and they underwent a general physical and neurologic examination to confirm their general good health. None had a history of neurologic, psychiatric, or cardiovascular diseases. The mean age of the group was 62.4 ± 13.4 years; 61% were female. Fourteen of these patients were included in our other study [9].

### *SPECT Scanning and Interpretation*

*SPECT technique.*—SPECT was performed with the ASPECT scanner (Cambridge, MA), a digital SPECT system with a single-crystal sodium iodide ring detector and three collimators designed to view the patient's head from three orthogonal angles simultaneously. The scanner had a center resolution of 7 mm. All patients had 25–30 mCi (925–1110 MBq) of the perfusion agent $^{99m}$Tc–hexamethylpropyleneamine oxime (HMPAO) (Ceretec, Amersham Corp., Arlington Heights, IL) injected while they lay supine in a dimly lit, quiet room. Imaging began 10 min after injection, and the acquisition time was 30 min. Standard techniques of acquisition and reconstruction were used [13]. Each data set was reconstructed in axial, coronal, and sagittal planes. For purposes of analysis, images were displayed on a color monitor in the axial plane. Five axial 1.67-mm slices were summed to provide approximately 14 images, each with a slice thickness of 8.3 mm. The color display level was individually adjusted for each patient so that the deep nuclei of the cerebellum were white (greater than 90% of the maximum activity of the slice), thus normalizing the entire data set to the $^{99m}$Tc-HMPAO activity of the cerebellum. For evaluation of the differences in uptake in different brain regions, the axial images of the 124 subjects were randomized and interpreted by three observers who had no knowledge of the clinical information. The three radiologists simultaneously reviewed each image and came to a consensus about the presence and location of any defects. The number of defects was evaluated in each of eight different regions of the brain: the lateral frontal cortex, medial frontal cortex, lateral temporal cortex, medial temporal cortex, parietal cortex, occipital cortex, basal ganglia (including caudate nucleus and putamen), and thalamus (Fig. 1). A defect was defined according to stringent criteria as a region of less than 60% of the maximum activity, greater than 1 cm in diameter, and spanning the full thickness of the cortex.

The midcerebral uptake index (MCUI), an objective measurement reflecting radionuclide uptake in the brain, was calculated by first adding the data obtained from three sequential 5-mm axial sections to yield a 1.5-cm slab centered at the thalamus; this slab included portions of the frontal, temporal, parietal, and occipital lobes, as well as the caudate nucleus and putamen. A large region of interest (ROI) was drawn around the cortex to include gray and white matter. The counts from this large ROI were divided by the number of picture elements (pixels) to calculate the counts per pixel for the midcerebral slab. Following this, an axial 5-mm slice through the midcerebellum was selected, and an ROI was drawn to include only the cortex of both cerebellar hemispheres; the counts per pixel of the cerebellar cortex in this slice was then calculated. To calculate the MCUI, we divided the counts per pixel of the midcerebral slab by the counts per pixel of the cerebellar cortex (Fig. 2).

*Statistical tests.*—Comparisons between the groups according to age and sex were made by using analysis of variance. Because age and sex varied across all four groups, all subsequent analyses were adjusted for these factors. The primary analysis compared the four groups of patients in terms of the number of defects noted in each brain region from subjective image interpretation and in terms of the MCUI.

Initial analysis revealed no effect with respect to hemisphere location of defects, so the number of defects in each brain region was summed over both hemispheres. We performed multiple linear regression analyses by using PROC GLM of SAS software (PC ver-

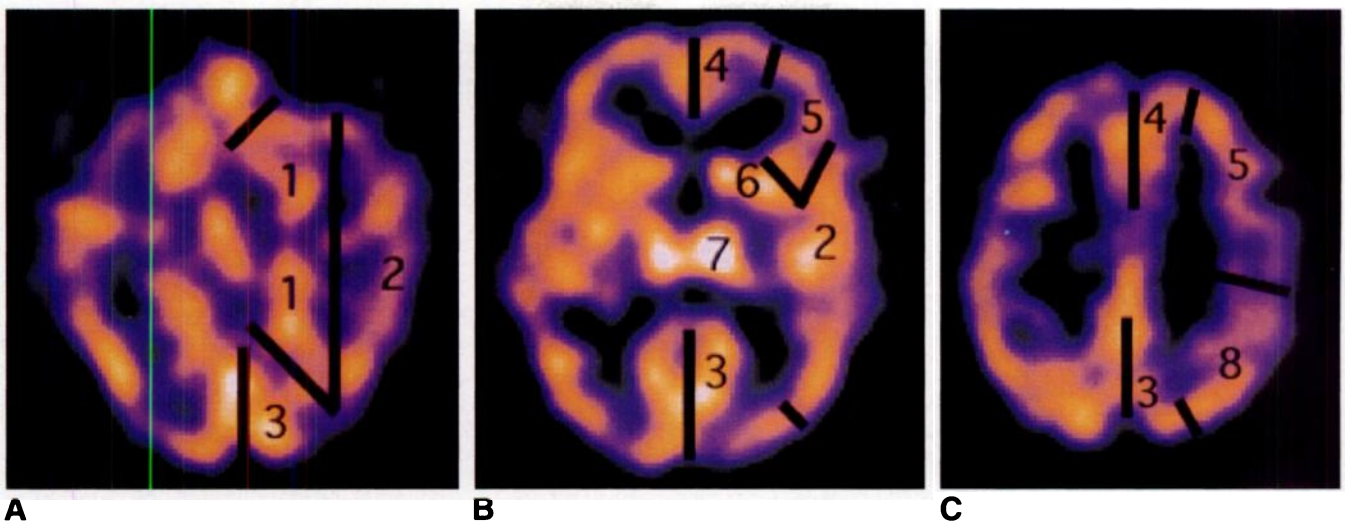


**Fig. 1.—*A–C*, Regions of interest (ROIs) on SPECT images of a patient with chronic fatigue syndrome. Axial images at three levels show the eight ROIs used in analysis: (1) medial temporal cortex, (2) lateral temporal cortex, (3) occipital cortex, (4) medial frontal cortex, (5) lateral frontal cortex, (6) basal ganglia (including caudate nucleus and putamen), (7) thalamus, and (8) parietal cortex.**

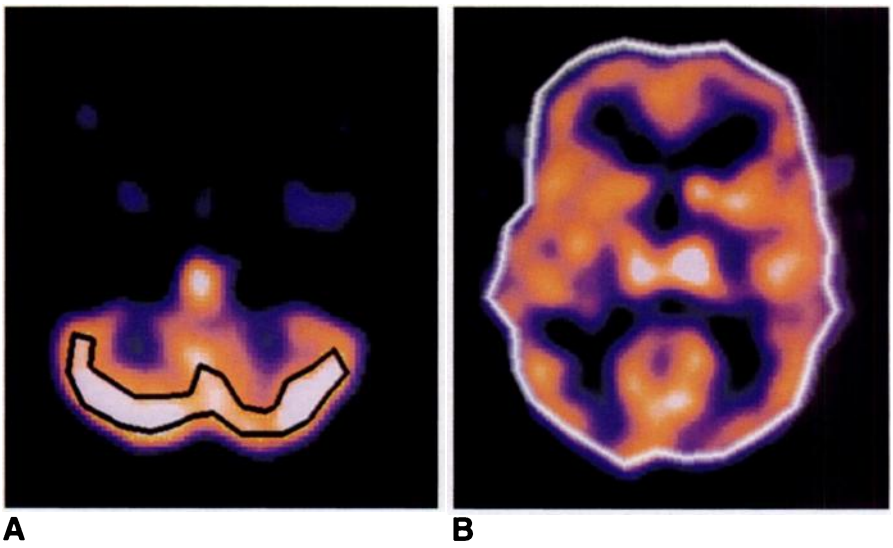


**Fig. 2.—*A* and *B*, Axial SPECT images of a patient with chronic fatigue syndrome show regions of interest (ROIs) used to calculate midcerebral uptake index (MCUI). ROIs have been drawn around cerebellar cortex of a 5-mm section obtained at midcerebellar level (*A*) and around perimeter of a 1.5-cm slab obtained at midcerebral level (*B*). Counts per pixel of midcerebral ROI were divided by counts per pixel of cerebellar ROI to yield the MCUI.**

sion 6.03), in which the number of regional defects was the dependent variable and the group of patients was the independent variable, adjusting for age and sex. Defect counts were log transformed when necessary to achieve a normal distribution. Results are presented as least-squares means and variance (standard deviation). Adjustment for multiple comparisons for regional defect analysis and MCUI was made by using the Student-Newman-Keuls option [14]. Correlation between the MCUI and the number of regional defects was determined by using the Spearman rank-correlation test. In comparing proportions (such as the frequency of various symptoms) between two groups, the $\chi^2$ statistic (or Fisher's exact test when cell sizes were less than five subjects) was used.

In all cases, significance was judged at the level of $p$ less than .05, two-tailed. Adjustment of the $p$ value in assessing alpha error was performed according to the method of Tukey [15]. Sex and age were used as covariates in the statistical analyses.

## Results

### *Representativeness of CFS Cases*

The 45 patients with CFS who were studied with SPECT and MR imaging were similar to the other 206 subjects (of the total of 251 who met at least one case definition for CFS) who were not studied radiologically with regard to age, sex, and severity of illness. There was a similar frequency of almost all neurologic symptoms, including headache, visual disturbances, difficulty with concentration, and seizures, between the groups that did and did not have SPECT ($p > .05$ for all differences, by $\chi^2$-test). On only two measures was there a significant difference between the groups that did and did not have SPECT: the duration of illness was somewhat shorter in the group that had SPECT vs the group that did not have SPECT, and there was a more frequent history of ataxia in the SPECT group vs the non-SPECT group. Thus, except for these two differences, the 45 patients studied with SPECT were representative of the larger group from which they were selected.

### *Comparison of Age and Sex Across the Four Patient Groups*

The subjects in the major depression and healthy comparison groups were similar in age and significantly older ($p <$

.001) than the subjects in the CFS and ADC groups. There were significantly fewer females in the ADC group than in the other three groups ($p < .001$).

The multiple regression analyses performed did not indicate an independent effect of age on either the number of defects or the MCUI. However, the relatively small number of younger subjects in the depression and control groups and the small number of females in the ADC group greatly limited the power of the analyses to detect such differences by age or sex.

*Regional Defects in Uptake*

The total number of defects per patient in each illness subgroup was significantly different from that of healthy controls: patients with CFS, 6.53 ± 4.94 (mean ± SD); patients with unipolar depression, 6.43 ± 5.61; patients with ADC, 9.15 ± 6.43; control subjects, 1.66 ± 2.60 (all $p < .005$). The ADC patients had significantly more defects than CFS patients ($p < .05$). In each of the eight regions, the smallest number of defects was seen in the healthy comparison group. The number of defects per patient was greater in the CFS group than in the healthy group in three of the regions (lateral frontal lobe, 1.71 ± 1.75 vs 0.21 ± 0.66; lateral temporal lobe, 1.67 ± 1.73 vs 0.39 ± 0.79; and medial temporal lobe, 1.11 ± 0.93 vs 0.42 ± 0.64). In patients with unipolar depression, defects in the lateral frontal (1.36 ± 1.50), lateral temporal (1.43 ± 1.60), and medial temporal (1.08 ± 1.07) lobes, as well as the occipital lobe (1.06 ± 1.64 vs 0.32 ± 0.77), were significantly greater than in normal subjects. In patients with ADC, the number of defects was significantly greater than in control subjects in the lateral frontal (2.30 ± 2.28), lateral temporal (2.04 ± 2.18), and medial temporal (1.59 ± 0.69) regions, as well as in the medial frontal lobe (0.67 ± 1.00 vs 0.00); there was also a trend toward significance in the occipital (0.93 ± 1.07) and parietal (0.78 ± 1.07 vs 0.18 ± 0.61) lobes. Thus, all three groups had significantly more defects than control subjects did in the lateral frontal, lateral temporal, and medial temporal lobes. Figure 3 shows SPECT scans of a patient with CFS, Figure 4 shows SPECT scans of a patient with ADC, Figure 5 shows SPECT scans of

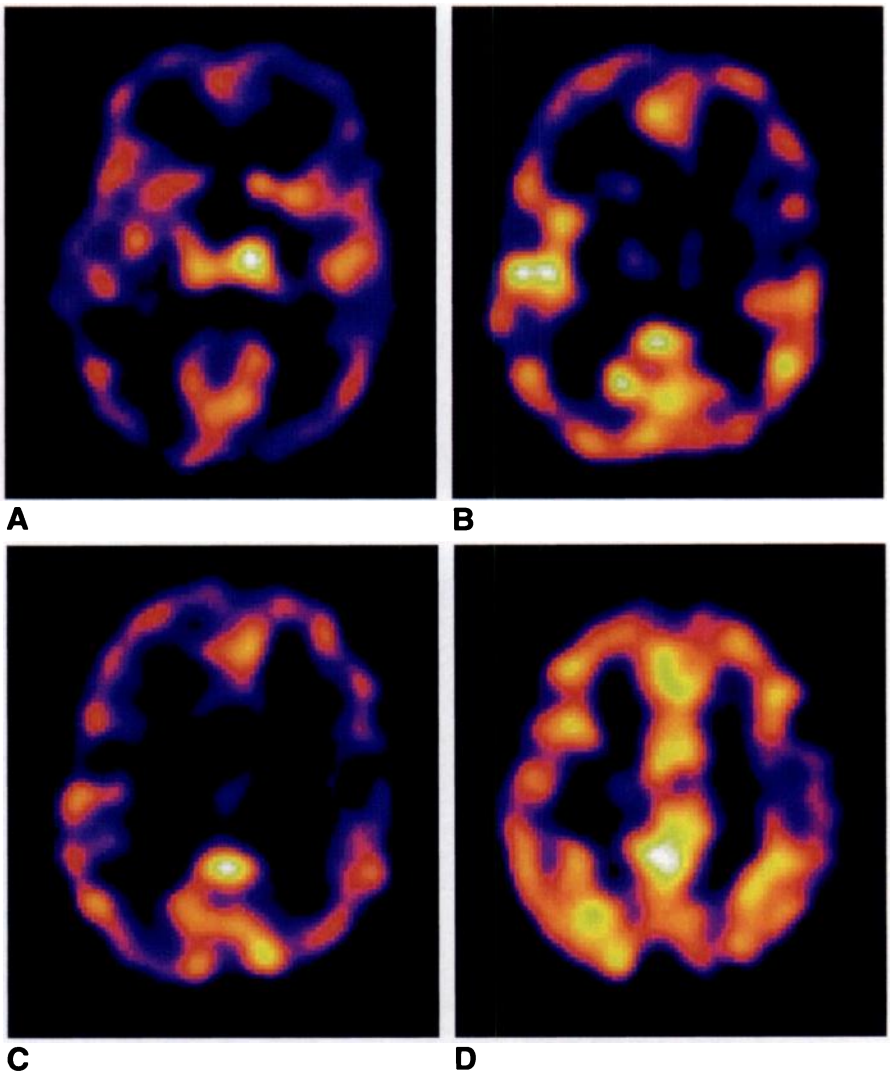


**Fig. 3.—*A–D*, Axial SPECT images (5-mm-thick sections) of a 42-year-old woman with chronic fatigue syndrome. Color scale ranges from black (low activity) to white (high activity). Multiple perfusion defects are present throughout the brain.**

a patient with unipolar depression, and Figure 6 shows SPECT scans of a healthy control subject.

### *Midcerebral Uptake Index*

The MCUI was significantly different across all four groups. In particular, the index was significantly reduced in the CFS (.667 ± .06) and ADC (.650 ± .05) groups, in comparison with the depression (.731 ± .16) and healthy (.716 ± .09) groups ($p < .002$). There were significant differences in the MCUI between patients with CFS and control subjects ($p < .005$) and depressed patients ($p < .025$), and between patients with ADC and control subjects ($p < .002$) and depressed patients ($p < .02$), but not between patients with CFS and ADC ($p < .2$) or between control subjects and depressed patients ($p < .8$).

The average counts per pixel in each midcerebral slab were also analyzed and were similar in patients with CFS (131.8 ± 80.2) and ADC (105.8 ± 70.2), and these values were both significantly reduced compared with those of control subjects (206.9 ± 137.0, $p < .005$); values in patients with depression (195.0 ± 198.2) were not significantly different from those in control subjects. Although the counts per pixel were significantly different between patients with ADC and depression ($p < .005$), the difference between patients with CFS and depression did not reach significance ($p < .075$).

There was a significant negative correlation between the MCUI and the total number of regional defects in the CFS group (Spearman coefficient, –0.41; $p < .005$) and the ADC group (Spearman coefficient, –0.44; $p < .025$), but no such correlation was noted in the depression or normal control comparison groups.

Unfortunately, detailed clinical information was not recorded on the days when the SPECT scans were obtained in the majority of patients. Thus, it was not possible to correlate SPECT findings with clinical status in any of the groups of patients.

## Discussion

This study demonstrates that CFS shares some similarities on SPECT imaging with both ADC and unipolar depression. The CFS and major depression groups had a similar

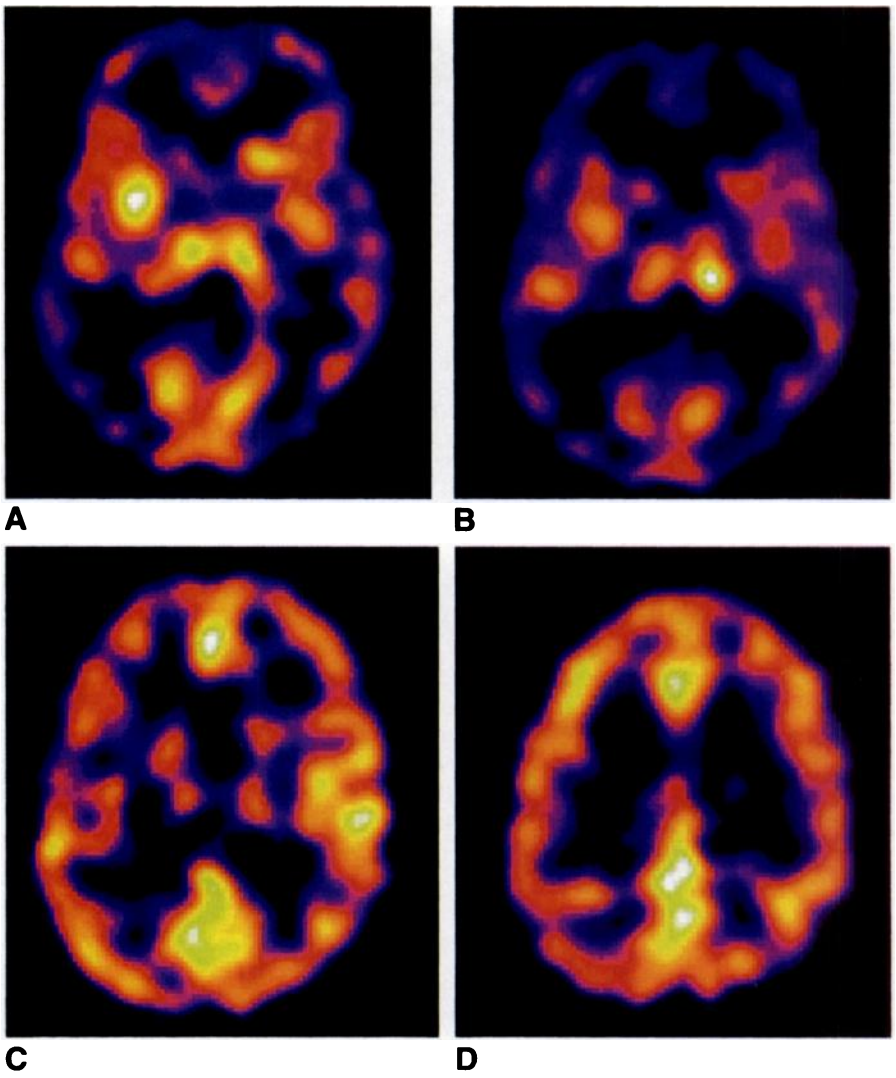


**Fig. 4.—*A–D*, Axial SPECT images of a 37-year-old man with AIDS dementia complex. Multiple perfusion defects are present throughout brain.**

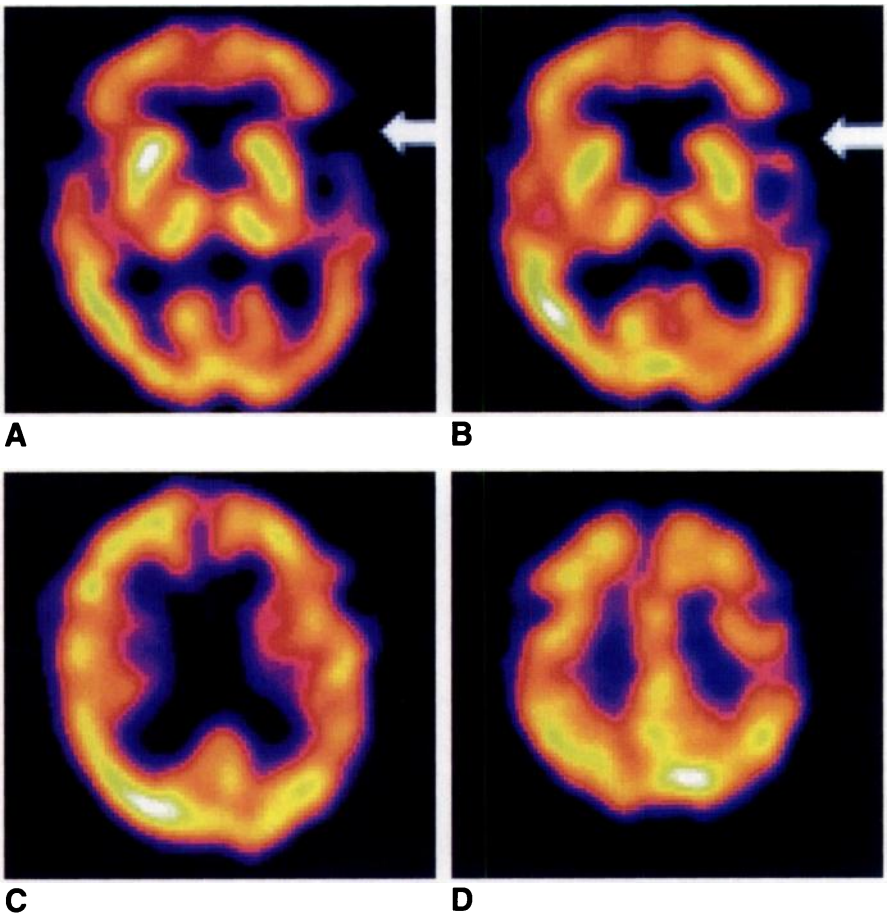


**Fig. 5.—*A–D*, Axial SPECT images of a 61-year-old woman with unipolar depression. Focal decreased radionuclide uptake is present in left lateral frontal and temporal lobes (*arrows*). Remainder of brain appears normal.**

number of regional defects, significantly greater than that in the healthy comparison group but less than in patients with ADC. Patients with CFS, ADC, and depression all had multiple defects that were most prevalent in the frontal and temporal lobes. The reason for the susceptibility of these regions is unclear, but it seems likely that the similarity in defect location may account for various cognitive and affective symptoms (depression, irritability, and decreased memory and mental capacities) common to patients in the three groups.

The MCUI, however, was significantly lower in patients with CFS and ADC than in patients with major unipolar depression or the healthy comparison group. By this objective standard, the pathophysiologic process in the CNS of patients with CFS would seem more similar to that in patients with ADC than that in patients with unipolar depression. Moreover, the MCUI values correlated with the regional defect count in the CFS and ADC groups, but not in the depressed patients or control subjects. As patients with CFS had as many regional defects as the depressed patients, this finding does not reflect merely an additive effect of the total defect count on overall uptake values. More likely interpretations of these data are that either the individual defects in the CFS and ADC groups were of greater severity than those in the depressed and normal groups, or the radionuclide uptake was reduced globally in the CFS and ADC patients, even in areas apparently free of focal defects. The distinction between these two possibilities would require determination of semiquantitative uptake values in defects and in surrounding tissue; although this was not possible in the present study, we are currently working to resolve this important issue.

The use of defect count data to determine regional prevalence of radionuclide uptake defects is a very conservative approach. Ichise et al. [16] performed a semiquantitative analysis using $^{99m}$Tc-HMPAO SPECT and reported decreased uptake in the frontal and temporal lobes, and to a lesser degree in the parietal and occipital lobes and basal ganglia. However, in our analysis, we required the intensity of a defect to be less than 60% that of normal brain, whereas Ichise et al. reported regional differences on the order of 10%; also, for purposes of analysis, we considered all defects, regardless of size, as single defects, which may have tended to underestimate the severity of SPECT abnormalities.

The pathophysiologic basis for the SPECT abnormalities noted cannot be determined from this study. A decrease in regional or global uptake on SPECT images may reflect an abnormality anywhere along the path of uptake of the radioiso-

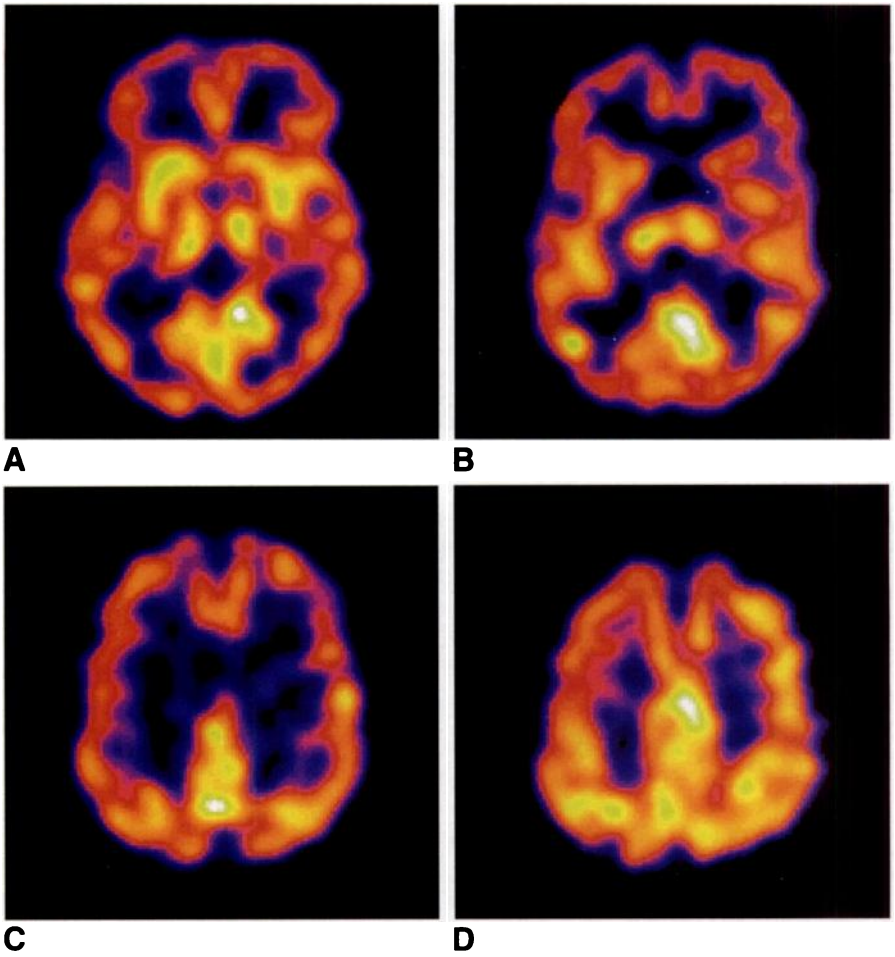


**Fig. 6.—*A–D*, Axial SPECT images of a 69-year-old male control subject show no abnormalities.**

tope, from the vascular delivery of the isotope to brain cells, transport of the tracer into the cells, and retention of the $^{99m}$Tc-labeled HMPAO moiety within cells so that images can be obtained. Therefore, an abnormal appearance of the brain on SPECT may represent hypoperfusion and/or cellular dysfunction at the cell membrane, cytoplasmic, or even nuclear level. Importantly, it is not necessary to invoke a single cause for the decreased radiotracer activity in the three different groups of patients or in the healthy control group. For example, whereas acute changes in radionuclide uptake in the younger population may be caused by inflammatory processes at the cellular or microvascular level, some foci of decreased uptake in older patients may reflect variation in cerebral perfusion due to focal or diffuse ischemic changes from chronic silent cerebrovascular disease [17]. Indeed, the findings on SPECT are nonspecific, and multiple regional perfusion abnormalities also have been seen in such diverse conditions as systemic lupus erythematosus [18], cocaine abuse [11, 19], and multiinfarct dementia [20]. The SPECT findings in this study therefore should not be considered to be primarily of diagnostic importance, but rather as descriptive data that may be helpful in elucidating the disease processes in each disorder.

Patients with unipolar depression had defects localized primarily to the frontal and temporal lobes, in agreement with previous reports [21–23]. The similarity in the location and number of defects in patients with major depression and CFS may pertain to the clinical similarity of patients with these disorders; however, the differences in MCUI between these conditions implies a qualitative difference in the pathophysiology of the CNS defects in the two conditions. The normal MCUI values in depressed patients militates against the presence of a diffuse inflammatory or vasculitic process. Instead, focal abnormalities throughout the cortex in these patients may reflect decreased cortical activity in subcortical projection sites owing to reduced neurotransmitter release [23, 24] without intrinsic cellular dysfunction. Alternatively, focal ischemic changes involving the frontotemporal regions may be responsible for late-onset depression in elderly subjects [22, 24]; the presence of additional posterior cerebral defects in the depressed subjects suggests that these patients may have experienced widely distributed small infarcts, and the defects in the frontal and temporal regions may have predisposed them to development of late-onset depression. Indeed, it is likely that small subclinical infarcts caused the few focal radionuclide uptake defects noted in our elderly control subjects.

As has been reported in previous SPECT and autopsy studies, patients with ADC in our series had multiple defects

throughout the brain, with prominent involvement of the frontal and temporal lobes [25–27]. The number of SPECT abnormalities in patients with ADC tended to be greater than in patients with CFS or depression. However, the similarity in MCUI data between patients with ADC and CFS suggests a similar origin for the neurologic dysfunction in these conditions. SPECT abnormalities in ADC are believed to be due to direct CNS infection by the HIV virus [11, 26, 28]. Pathologic studies have shown that HIV infection results in a subacute encephalitis characterized by demyelination and the presence of the virus in multinucleated giant cells, as well as in endothelial cells, astrocytes, and neurons distributed throughout the brain [28].

Although neuropathologic data in patients with CFS are unavailable, the findings in CFS are consistent with the hypothesis that CFS also results from viral infection of neurons, glia, or vasculature. Previous studies have suggested that Epstein-Barr virus [29], enteroviruses [30], retroviruses [31, 32], or the recently discovered human herpesvirus 6 [8], alone or in concert, may play a role in CFS. Viral infection can produce neuroglial dysfunction by interfering with intracellular mechanisms or membrane transport systems, by producing focal demyelination in association with circulating immune complexes [32, 33], or by cerebral hypoperfusion due to vasculitis.

This study has a number of limitations. Perhaps the most important is that the patients with major depression (mean age, 70.0 years) and healthy comparison subjects (mean age, 62.4 years) were considerably older than the patients with CFS (mean age, 43.3 years) and the patients with ADC (mean age, 39.6 years). It would have been preferable to study findings in depressed and healthy patients of ages similar to those of patients with CFS and ADC. Although we did not find evidence that age had an independent effect on the SPECT findings, our power to find such an effect was small. If increasing age were associated with diminished perfusion due to cerebrovascular disease, for example, this would have introduced a bias against recognizing differences between the younger CFS and ADC patients vs the older depressed and healthy patients.

A second limitation is that the comparison group with major depression was taken from an inpatient psychiatry service, and thus these patients were severely depressed. Patients with CFS (or unrecognized HIV encephalopathy) are more readily confused with ambulatory patients who have dysthymia or milder forms of unipolar major depression. The use of hospitalized patients with depression could have introduced a bias against recognizing differences between the patients with CFS and ADC vs the depressed patients. It also is possible that a concomitant reactive depression in patients with CFS and HIV infection, due to their chronic disability, could have independently affected the results of the SPECT study and confounded the ability to distinguish the CFS and ADC groups from the depressed group with SPECT. Because no formal psychiatric evaluation was performed at the time of SPECT scanning, our study cannot address this possibility.

Third, the calculation of the MCUI involved the assumption that cerebellar uptake was normal in all patients. There was no direct evidence to the contrary, but subtle decreases in uptake may have affected the MCUI calculations without being manifest in our regional defect count analysis. However, if cerebellar uptake was actually reduced in our groups of patients, the result would be a calculated uptake ratio higher than was actually present, introducing a conservative bias that would have obscured any differences between the groups of patients and normal control subjects. Furthermore, we found that analysis of the average counts per pixel at the midcerebral level (independent of cerebellar counts) resulted in findings similar to those of the MCUI analysis.

In summary, this study indicates that SPECT may help in distinguishing patients with CFS from healthy subjects and depressed patients. SPECT was not useful in separating patients with CFS from patients with ADC, but that distinction usually can be made with other diagnostic technologies; moreover, the similarity in the appearance on SPECT suggests the possibility of similar underlying abnormalities in ADC and CFS. However, given the limitations cited here, we intend further studies to determine the value of SPECT in the differentiation of CFS from other encephalopathic conditions. These will include precise mapping of MR and SPECT abnormalities, longitudinal studies, correlation of radiologic abnormalities with clinical information, and most important, using objective regional uptake indexes instead of subjective defect counts to evaluate focal changes on SPECT. These efforts may help us to establish more accurately the diagnosis and prognosis in individual cases of CFS, and ultimately to understand more fully the pathogenesis of the syndrome.

## ACKNOWLEDGMENTS

We thank John Orav and Marie Kijewski for statistical advice; Keith Johnson for recruitment of healthy subjects; Marilyn Albert for recruitment of depressed patients; and Jack Mendelson, Elizabeth Hallgring, Siew Koon Teoh, Jonathan Worth, and Bradforfd Navia for recruitment of patients with ADC.

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