A Comparison of Brain Perfusion SPECT in Cocaine Abuse and AIDS Dementia Complex

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Intravenous drug use is a major risk factor for HIV-1 infection. Since both AIDS dementia complex (ADC) and cocaine have been associated with abnormal brain perfusion imaging, we compared the scintigraphic patterns of ADC patients and cocaine polydrug users with normal control subjects using ^{99m}Tc-HMPAO SPECT. We found a high incidence of cortical defects in both ADC (100%) and cocaine-dependent (90%) subjects. In the cocaine and ADC patients, cortical defects were most frequent in the frontal, temporal and parietal lobes and occurred with similar frequency in the two populations. In both groups, the number of cortical defects per subject was higher than normal subjects (10.0 ± 5.0 for ADC, 10.1 ± 5.2 for cocaine and 0.7 ± 1.5 for normal), background activity was high (a 65% and 60% incidence for ADC and cocaine, respectively), and basal ganglia involvement was frequent (40% and 65% for ADC and cocaine). We conclude that the brain perfusion pattern, while a sensitive indicator of ADC, cannot be distinguished from chronic cocaine polydrug use and caution should therefore be applied before entertaining a specific diagnosis.

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AIDS dementia complex (ADC) is a devastating complication of HIV-1 infection (*1,2*). Its early detection may be difficult because other complications of HIV infection such as major depression, CNS opportunistic infection, and drug side-effects can mask the signs and symptoms of ADC. Brain perfusion SPECT is a sensitive diagnostic technique even in early ADC (*3–5*). Unfortunately, perfusion defects also occur frequently in chronic cocaine polydrug users (*6–7*), a group at high risk for HIV infection. By using ^{99m}Tc HMPAO SPECT to determine whether the perfusion patterns of ADC and cocaine dependence can be differentiated, we compared the scintigraphic patterns in three groups of subjects: ADC patients, chronic cocaine polydrug users and normal control subjects.

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METHODS

Study Populations

The study population consisted of 20 cocaine-dependent subjects, 20 patients with ADC and 20 normal control subjects. The cocaine-dependent subjects were males with a mean age of 31.6 yr (range: 22–43). All subjects tested negatively for the HIV-1 antibody, met DSM-III-R criteria for current cocaine abuse or dependence and had used cocaine within 2 days of SPECT imaging. The cocaine-dependent subjects used other substances: cannibus (8 subjects), alcohol (20 subjects), opioids (13 subjects) and other substances (9 subjects). The subjects with ADC met American Academy of Neurology criteria for HIV-1 associated cognitive/motor complex (*8*). They were all males with a mean age of 35.7 yr (range: 25–61). Their Centers for Disease Control group classifications were II (three subjects), III (two subjects), IVa (six subjects), IVb (one subject), IVc (six subjects), and IVd (two subjects) (see Appendix). The control subjects consisted of seven males and thirteen females and had a mean age of 64.7 yr (range: 55–78). They underwent a general physical examination and an extensive neurologic interview and examination. None had histories of neurologic, psychiatric or cardiovascular diseases and all had normal neurologic examinations.

The patients were studied using an annular single crystal brain camera (ASPECT), a digital SPECT system with a single-crystal sodium iodide ring detector and three collimators designed to view the patient's head from three angles simultaneously (*9*). All patients were injected with 20 mCi of ^{99m}Tc-HMPAO while supine in a dimly lit room with background computer fans serving as white noise. Imaging began 10 min after injection with an acquisition time of 30 min (15 sec per projection) in 120 projections with a 360° rotation of the collimators. Two pulse-height analyzer windows were employed, one set at 140 ± 14 keV and one set to acquire scatter information from 112 to 126 keV. The combined set of projections were then corrected by subtracting 90% of the scatter projections and filtered to remove the forward scatter component from the photopeak projections. The projections were smoothed using a Butterworth filter (cutoff = 1.05 cycles per cm; power factor = 10), and then backprojected using a ramp filter. The reconstructed slices were corrected for attenuation using an attenuation factor of 0.15 cm and displayed on a 128 × 128 matrix (1.67 × 1.67 mm) as a set of 64 slices (1.67 mm slice thickness).

Each data set was reconstructed and displayed on a color monitor in axial, coronal and sagittal planes. Five 1.67-mm slices were summed to provide approximately 14 images, each with a slice thickness approximately equivalent to the spatial resolution of the instrument (8.3 mm). The monitor display format consisted of a 16-component color scale, with white representing the maximum of reconstructed activity. The color display level was individually adjusted for each patient so that the central area of the cerebellum was white (greater than 90 percent of the maximum activity of the slice), thus normalizing the entire data set to the ^{99m}Tc-HMPAO activity in the cerebellum. Images were classified as abnormal if a region of cortical activity had less than 60% of the maximum activity (absence of white, yellow or red in an area of cortex on two or more slices) or if basal ganglia uptake was asymmetrical (a difference of one or more color levels between the left and right sides) or less than 60% of maximum activity. Background activity was considered abnormally high if soft-tissue activity was greater than 20% of maximum activity (cerebellum) on a transaxial image at the level of the basal ganglia (appearing as a blue halo about the brain on the color-coded images).

The transaxial images were interpreted by two readers blinded to the clinical information. Focal perfusion defects were recorded as to location (frontal cortex, temporal cortex, parietal cortex, lateral occipital cortex, primary visual cortex, basal ganglia, and thalamus). In addition, focal areas of increased activity were recorded as to location. Soft-tissue background activity was recorded as abnormal if it was equal to or greater than 20% of maximum activity over the entire circumference of the head.

Nominal data (number of patients with defects) were tested for significance using the chi square test statistic. Continuous data (number of defects per patient) were analyzed using the Student-Neumann-Keuls test for multiple comparisons.

RESULTS

The fraction of patients with cortical defects was similar for ADC and cocaine subjects (100% versus 90%) and was significantly greater than for normal subjects ($p < 0.01$) (Fig. 1). The fraction of patients with cortical defects in either the frontal, temporal or parietal cortex was similar for the two abnormal groups and was significantly higher than controls in each of the regions ($p < 0.01$) (Fig. 2). There were more defects on the left side in both abnormal groups (64.6% for ADC versus 61.2% for cocaine).

The total number of cortical defects per subject was similar for the two groups (10.0 ± 5.0 for ADC versus 10.1 ± 5.2 for cocaine) and was significantly greater than for normal subjects (0.7 ± 1.5) ($p < 0.01$) (Fig. 3). The frequency of cortical defects was also significantly greater for the two abnormal groups than for the normal control subjects in three of the cortical regions (frontal, temporal and parietal) ($p < 0.01$) but was similar for the cocaine-dependent and ADC subjects. The incidence of increased background uptake was also similar for the abnormal groups but was greater than that for the normal subjects (65% and 60% versus 5%) ($p < 0.01$). No cortical defects were observed in either group in the primary visual cortex and cerebellum. While the incidence of abnormal basal ganglia uptake was slightly greater in cocaine-dependent

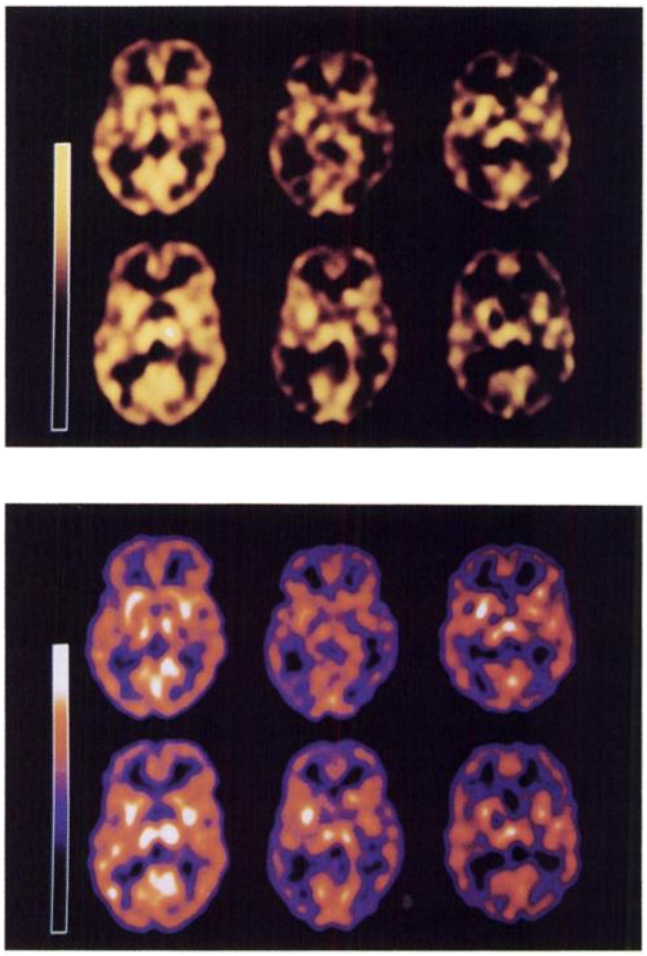

FIGURE 1. Transaxial images of a normal subject (left), a cocaine dependent subject (middle), and an ADC subject (right) using color tables to accentuate functional anatomy (A) and to reflect our schema for visual quantitation (B). Both the cocaine-dependent and ADC subjects had multiple bilateral cortical and basal ganglia defects. The cortical defects involved the frontal, temporal and parietal lobes.

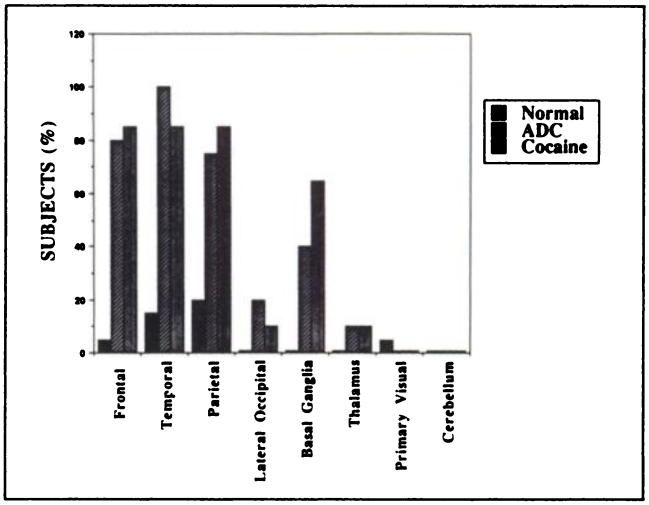

FIGURE 2. Number of subjects with focal perfusion defects.

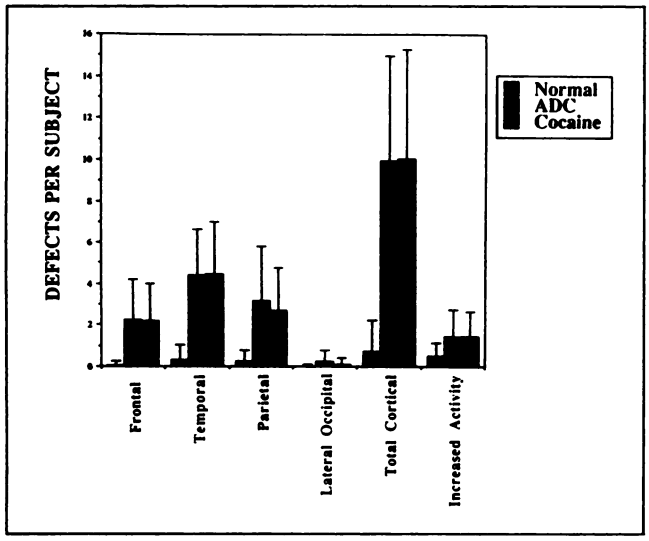

FIGURE 3. Number of focal cortical perfusion defects per subject.

subjects than ADC subjects, the difference did not attain statistical significance (40% versus 65% for ADC and cocaine subjects, respectively). The number of foci of increased activity per subject activity was also greater for both ADC and cocaine subjects than normal controls (1.5 ± 1.3 and 1.5 ± 1.2 versus 0.6 ± 1.5) ($p < 0.01$).

DISCUSSION

Both ADC and cocaine use have been associated with multiple focal cortical defects on brain perfusion imaging. Perfusion defects on [^{123}I]IMP SPECT images have been associated with chronic occasional cocaine use (*6*). With high-resolution SPECT imaging, perfusion defects among cocaine polydrug users were noted to be primarily small and multiple involving the frontal, temporal, and parietal cortex and basal ganglia (*7*). Brain perfusion SPECT in patients with ADC has been performed primarily with single-head gamma cameras (*3–5*). A high incidence of abnormalities has been demonstrated in these patients using brain perfusion even in patients with early disease.

The incidence of HIV-1 infection among intravenous drug users is very high, ranging from 40% to 60% of the population at risk (*10*). The usefulness of brain perfusion SPECT in the early diagnosis of the ADC depends not only on its sensitivity in early disease, but also on its specificity with regard to other diseases that occur in the population at risk. We find that the pattern of uptake is similar for cocaine users and ADC patients. Multiple focal cortical perfusion defects are found in approximately equal frequency in the frontal, parietal and temporal cortex in both groups. Basal ganglia abnormalities are also found in both groups.

Background activity is also increased equally in the two groups. The apparent increase in background activity reflects a true reduction in tracer uptake to the brain. This generalized decrease in ^{99m}Tc-HMPAO uptake in both cocaine-dependent and ADC patients may be due to a generalized decrease in brain blood flow or a decreased retention of the tracer, perhaps due to increased porousness of the blood-brain barrier or to reduced glutathione concentration (*11*). While our study does not offer an explanation for the reduced brain uptake of ^{99m}Tc-HMPAO, relative brain-to-background activity is a useful indicator of disease in patients who might be at risk for substance abuse or HIV infection.

While some heterogeneity is seen in cortical ^{99m}Tc-HMPAO uptake in normal subjects and probably represents the complex anatomic distribution of cortex over the brain surface and within sulci, the incidence of focally increased uptake is much greater in ADC patients and cocaine users than in the normals subjects. Increased tracer uptake may represent small focal areas of luxury perfusion due to microinfarcts, an altered blood-brain barrier with increased uptake, and/or retention of the tracer in areas of functional damage. While conventional MRI and CT studies are normal in most of these patients, autopsy results in HIV-1 infected subjects show a high incidence of diffuse and focal brain disease, including the presence of multinucleated cells and white matter pallor with astrocytic proliferation (*12,13*). In addition, perivascular infiltrates are a frequently associated finding in ADC (*14*). Indirect mechanisms of brain injury may contribute to the development of functional changes, including the release of neurotoxic agents by infected macrophages (*15,16*). Direct mechanisms may involve the viral glycoprotein envelope itself (*1–5*). These changes in cerebral function may be coupled with cerebral perfusion and affect either apparent background activity or uptake and retention of the tracer within the brain. Much less is known about the effect of cocaine on human brain micromorphology, although the vasoconstrictive effects of the drug might result in similar processes (*17,18*).

Our cocaine-dependent subjects used other substances, particularly cannabis, and alcohol but all of the subjects tested negatively for HIV-1 antibodies. None of the ADC patients were intravenous drug users and all denied cocaine use.

While brain perfusion SPECT appears sensitive in patients with early ADC and chronic cocaine use, the two scintigraphic patterns are similar and cannot be distinguished from each other. In addition to multiple focal cortical defects and reduced uptake in the basal ganglia, increased background activity and foci of increased tracer accumulation are scintigraphic signs that accompany both conditions.

APPENDIX

CDC Classification System for HIV-1 Infection

Group I	Acute infection (a mononucleosis-like syndrome, with or without aseptic meningitis, as-

	sociated with seroconversion for HIV-1 antibody)
Group II	Asymptomatic infection
Group III	Persistent generalized lymphadenopathy
Group IV	Other disease
Subgroup A	Constitutional disease (e.g., fever persisting more than 1 mo, involuntary weight loss of greater than 10% of baseline, or diarrhea persisting more than 1 mo, and not due to other illness)
Subgroup B	Neurologic disease (dementia, myelopathy, or peripheral neuropathy, not due to other illness)
Subgroup C	Specified secondary diseases (listed in the CDC surveillance definition for AIDS, 1987 revision)
Subgroup D	Secondary cancers (Kaposi's sarcoma, non-Hodgkin's lymphoma or primary lymphoma of the brain)

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