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BACKGROUND AND PURPOSE: **This study was designed to determine whether neuropsychological function in HIV-infected persons is correlated with loss of brain volume (as measured by percentage of brain parenchymal volume [PBV]). We hypothesized that whole-brain parenchymal volume might correlate with neuropsychologic performance, even before overt clinical dysfunction is apparent.**

METHODS: **A computer-assisted segmentation technique with thin section MR imaging was used for 15 patients with HIV infection (seven symptomatic, eight asymptomatic) and for five HIV-negative control participants to quantify whole brain and CSF volumes. To determine the degree of brain atrophy, the PBV relative to that of intracranial content was calculated. Neuropsychological performance was assessed by using a standard battery of eight tests (NPZ-8 test battery).**

RESULTS: **HIV-infected patients had significantly lower NPZ-8 scores ($t[18] = 2.26$, $P < .05$) and lower PBV ($t[18] = 1.79$, $P < .01$) than those of healthy control participants. With the Spearman rank order correlation coefficients, data analyzed for all 20 study participants (15 HIV-infected patients and five noninfected control participants) showed a significant ($r = -0.50$, $P < .05$) negative correlation between PBV and NPZ-8 test battery score. In addition, there was a significant negative correlation between subtest score of motor impairment and PBV ($r = -0.69$, $P < .01$) and between AIDS dementia complex score ($r = -0.64$) and PBV ($P < .01$).**

CONCLUSION: **These correlations suggest that quantitation of PBV may offer an objective, easily acquired surrogate predictor of neuropsychological impairment and clinically apparent cognitive/motor dysfunction among HIV-infected persons.**

AIDS dementia complex (ADC) is an HIV-associated chronic, neurodegenerative syndrome afflicting 15–20% of patients with AIDS. It is characterized by progressive cognitive impairment and brain atrophy (1). The diagnosis of ADC requires the clinical indication of CNS neurologic dysfunction in addition to objective measures of dysfunction on standardized neuropsychological tests, typically the NPZ-8 test battery (2). The virus enters the brain early after systemic infection is established, and progressive neurodegeneration occurs as a result of viral replication within the cells of the macrophage lineage (3–5). The most common neuroradiologic brain abnormality in patients with ADC is atrophy; the next most common are white matter lesions (6). ADC is usually diagnosed during the later stages of AIDS (1, 7), and clinical symptoms include the presentation of subcortical features of inattention, indifference, and psychomotor slowing before the development of frank dementia (8–10). Unfortunately, by the time functional impairment develops in patients, significant brain atrophy may have occurred, suggesting that clinical manifestations of cognitive impairment often herald significant irreversible structural brain damage and cellular loss (11). It is critical, therefore, to develop objective measures of neurodegeneration that can potentially identify patients who are at risk for development of irreversible structural and functional impairment.

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This study was designed to determine whether a correlation exists between the loss of brain volume (as measured by the percentage of brain parenchymal volume [PBV]) and neuropsychological functioning in HIV-infected persons. The PBV corrects for variability in the size of the intracranial contents. By measurement of the whole brain volume, the sampling bias of regional sampling techniques is avoided. We hypothesized that because HIV degeneration is a diffuse disease process, analysis of the entire brain parenchyma would provide a correlate for neurocognitive measures. We further hypothesized that because HIV infection of the CNS occurs early after initial systemic infection, loss of brain parenchymal volume may occur in infected persons before overt clinical manifestations of ADC are apparent.

Methods

Participants

Fifteen patients who had seropositive results for HIV-1 (12 men, three women; eight neurologically asymptomatic, seven neurologically symptomatic) and five age-matched neurologically healthy control participants were enrolled in this study. The term neurologically symptomatic refers to patients who received ADC stage scores of ≥0.5 based on examination by a neurologist experienced in the diagnosis of ADC (D.L.K.) and neuropsychologic testing (NPZ-8 test battery) (1). Several additional neuropsychological tests were also conducted to determine whether groupings of neuropsychological subtests would offer additional correlates with the PBV. By the same criteria, the term neurologically asymptomatic refers to patients who received an ADC stage score of zero, indicating absence of clinical neurologic dysfunction, and normal NPZ-8 test battery results. The mean age of the HIV-symptomatic patients was 40.06 years (age range, 22–56 years), the mean age of the HIV-asymptomatic patients was 34.06 years (age range, 28–40), and the mean age of the healthy control participants was 36.52 years (age range, 21–65 years). The NPZ-8 scores of the patients ranged from 0 to 15, with numbers >0 indicating increasing levels of neuropsychological dysfunction. Eight patients who tested seropositive had an ADC stage score of 0, five had a score of 0.5, and two had a score of 1. All HIV-positive patients participating in this study were recruited from the immunodeficiency program at the University of Pennsylvania and were prescreened for risk factors for cognitive impairment before study entry. Exclusion criteria included a history of concussive head injury, long-term steroid use, stroke, brain mass, seizures, active psychiatric disorder, and active alcohol or substance abuse. Patients who were enrolled in this study were screened by means of medical and/or neurologic history taking and physical examination. No patients with active drug or alcohol abuse were included in the study. A history of either drug or alcohol use was not an exclusionary criterion for enrollment, which was conducted according to guidelines used by the AIDS Clinical Trials Group of the National Institute of Allergy and Infectious Diseases of the National Institutes of Health. All patients who had an ADC rating of ≥0.5 were enrolled in ongoing clinical studies for HIV-associated neurocognitive impairment through the AIDS Clinical Trials Unit of the University of Pennsylvania, which is part of the national AIDS Clinical Trials Group consortium. No patients were receiving corticosteroids, nor had any patients been receiving long-term corticosteroids.

All patients were deemed clinically stable, without progressive weight loss or constitutional symptoms, at the time of study entry. The study was approved by our institutional review board, and written informed consent was obtained from all patients and control participants.

MR Imaging

MR imaging was performed with a 1.5-T unit by using a quadrature transmit/receive head coil. All MR imaging examinations used fast spin-echo T2-weighted imaging with 2500/18/90 (TR/TE/effective TE), 3-mm-thick sections (contiguous, interleaved), 22-cm field of view, 256 × 192 matrix, >50 sections, echo train length of eight, and 0.86-mm pixel size. The first (intermediate-weighted) and second (T2-weighted) echoes of the fast spin-echo sequence in each study were then transferred electronically to our medical image processing laboratory, where the brain parenchymal volume and CSF volume were calculated. MR imaging of the brain was performed within 2 days of the neuropsychological examinations.

Image Processing

MR imaging data were transferred directly to the computer systems of the medical image processing group by means of a picture archiving and communication system. The images were processed by using an internal version of the 3DVIEWNIX (12) software system that was developed, maintained, and distributed by the Medical Image Processing Group of the University of Pennsylvania. All processing operations used to obtain the results reported herein were performed with a Sun Sparc 20 workstation (Sun Microsystems, Mountain View, CA) by a trained neuroradiologist (Y.G.). Lesion volume calculations were performed with a validated semiautomatic computerized method based on the concept of fuzzy connectedness by using two (intermediate-weighted and T2-weighted) image sets. This method has been described previously (13, 14) and validated in several studies (15–18) with more than 500 data sets. The known inter- and intraobserver variability for this method is <1% for the total lesion volume (17).

Parenchyma and CSF volumes also were determined with the 3DVIEWNIX system. The process began with the segmentation of the intracranial contents (17) after an operator briefly identified the gray matter, white matter, and CSF by specifying a few points in one section that was approximately centrally situated in the brain. All of the segmented sections (>50 in each study) were then reviewed, and any residual extracranial components were excluded, if need be, by the operator. This is the only processing step that requires manual interaction with each patient.

The CSF-only image was obtained with the whole-brain segmentation technique by using segmented T2-weighted and intermediate-weighted data sets. With this method (13, 14, 17), an angle image of CSF was created by using the following equation: $I_{angle} = \tan^{-1}(I_{T2}/I_{INT})$, where I_{angle}, I_{T2}, I_{INT} are the signal intensities of the voxels on the angle, T2-weighted, and intermediate-weighted images, respectively. The power of the angle image comes from the effective elimination of the wide variation in CSF signal intensities that are commonly seen on the T2-weighted and intermediate-weighted images because of inhomogeneity in the magnetic field. The resulting angle image has relatively homogenous CSF signal intensity values that can be effectively segmented with thresholding. The threshold value was selected by using the T2-weighted images to produce a CSF-only image, which accurately depicted the CSF volume. After normalization was achieved on the angle images, the threshold was fixed without requiring additional per-study adjustment. The CSF volume was calculated by summing the total volume of the voxels on the CSF-only image.

To normalize for baseline differences in brain parenchymal volume among patients and control participants, an additional parameter, the PBV, was calculated as the percentage of brain volume within the volume of the intracranial contents. PBV was calculated by dividing the brain parenchymal volume by the

sum of the brain parenchymal volume and CSF volume. To determine the reproducibility of the various volume estimations, we performed repeat MR imaging within 1 week after the previous imaging examination for 10 randomly chosen patients. The previously described parameters were used to obtain the repeat images. For the whole-brain parenchymal volume calculation, we included those sections from the MR image sets that started from the section just before the cerebellum appeared in the bottom and extended to the last section at the top of the brain.

Neuropsychological Evaluation

Neuropsychological assessments were performed by using a standard battery of eight tests (NPZ-8 test battery), including the California Computerized Assessment Package (Cal Cap) reaction time tests (2, 19, 20) and additional tests of memory, motor function, and mood, as listed below. The NPZ-8 test battery included the following: trail making A and B, digit symbol test, timed gait, grooved pegboard (dominant and nondominant hands), basic choice reaction time (Cal Cap), and sequential reaction time (Cal Cap). Overall Z scores were obtained by subtracting raw scores on individual tests from the reference group's mean scores and dividing the differences by the reference group's SD (2). Normal scores for each test were derived from the Multicenter AIDS Cohort Study HIV-negative sample group according to age and education level (21). The composite Z score (NPZ-8) represents the average of the individual Z scores for the eight tests. A composite Z score of ≥ 2 in addition to clinical criteria according to the Memorial Sloan Kettering Classification system was required for the diagnosis of ADC (22–24).

To attempt to develop better discriminate neuropsychological subtest sensitivity for our analysis, in addition to the NPZ-8 test battery, we used the following tests to develop composite scores in areas of total memory, processing speed, motor speed, and mood: 1) Rey Auditory Verbal Learning Test of attention and verbal memory; 2) Stroop Color Interference Test for abstraction and divided attentional abilities; 3) WAIS-R vocabulary to estimate level of intellectual functioning at study entry; 4) Profile of Mood States to assesses current mood state and disturbances; and 5) The Center for Epidemiological Studies Depression Scale, a self-reported measure of symptoms of depression. We used these tests in addition to subtest scores from the NPZ-8 test battery to derive composite scores in for total memory impairment, motor speed impairment, processing speed impairment, and total mood dysfunction. These composite scores were defined as follows: total memory = average sum of raw scores from five Rey Auditory Verbal Learning Test trials; motor speed score = sum of Z scores from timed gait, grooved pegboard dominant hand, and grooved pegboard nondominant hand; total mood score = sum of the subtest scores of the profile of mood states scores in areas of anxiety, depression, anger, vigor, fatigue, and confusion; processing speed score = sum of Z scores from trail making A, trail making B, digit symbol modalities, and Cal Cap computerized reaction time tests.

All neuropsychological testing was conducted by a nurse examiner (I.M.) highly experienced in ADC trials and trained and supervised by a clinical neuropsychologist (G.G.). The testing was conducted in a quiet room with minimal visual or audible distractions. Periods of rest were provided during testing to minimize the effects of fatigue.

To determine the relationship between PBV loss, HIV infection, and neurologic function, we examined subtest scores derived from our test battery and clinical ADC staging. The functional parameters we chose were ADC stage score, NPZ-8 score, and the following subtest groupings: total mood dysfunction score, total memory dysfunction score, processing speed (trail making A, trail making B, digit symbol modalities, and the Cal Cap computerized reaction time tests), and motor speed (timed gait, grooved pegboard dominant hand, and grooved pegboard nondominant hand).

Results

We assessed brain volume in 15 HIV-1-infected patients recruited from the Immunodeficiency Program at the University of Pennsylvania. Patients were classified as either neurologically healthy or impaired (ADC stage of ≥ 0.5) according to standard neurologic testing procedures (22). We also included five seronegative, neurologically healthy control participants. Patients underwent detailed neurologic examination, neuropsychological testing, and serologic studies for viral load and cluster of differentiation 4 T lymphocyte cell count. The average results from seven neurologically symptomatic (ADC stage, 0.5–1) patients, eight seropositive asymptomatic patients, and five seronegative normal control participants are presented in Table 1.

Note that for this study, we defined neurologically symptomatic patients as those with an ADC stage score >0. We realize that the designation minor cognitive motor disorder has been applied by some to patients with an apparent ADC stage score of 0.5.

Neuropsychological testing was performed by using standard neuropsychological tests as described in Methods. Standardization was performed by using the mean and SD for each test derived from the Multicenter AIDS Cohort Study HIV-negative sample group. For better discrimination of subtest sensitivity, we grouped the neuropsychological tests into three groups representing total memory impairment, motor speed impairment, processing speed impairment, and total mood dysfunction scores. Each ADC stage score represents a composite or average of scores for individual tests assessing that specific area of neurologic function. The ADC staging was determined according to standard neurologic criteria as described by the American Academy of Neurology (22, 23).

The 15 HIV-infected patients did not differ from the five healthy control participants with respect to age ($t[18] = 0.57$) or education ($t[18] = 1.53$). However, HIV-infected patients had significantly lower NPZ-8 scores ($t[18] = 2.26$, $P < .05$) and lower PBV ($t[18] = 1.79$, $P < .01$). We then examined Spearman rank order correlation coefficients to assess the degree of relationship between PBV and various indices of clinical function for all 20 participants.

Data analyzed for all 20 participants (15 HIV-infected patients and five noninfected control participants) showed a significant ($r = -0.50$, $P < .05$) negative correlation between PBV and NPZ-8 test battery score, as shown in Table 2. In addition, there was a significant negative correlation between subtest scores of motor impairment and PBV ($r = -0.69$, $P < .01$) and between the ADC stage score ($r = -0.64$) and PBV ($P < .01$). No significant correlations were found between total memory, processing speed, or total mood dysfunction scores and PBV.

TABLE 1: Brain volume and neuropsychological performance in HIV-1 patient cohort

Patient	Age (y)	Sex	CD4 (cells/μL)	Plasma RNA (copies/mL)	Brain Volume (cm^3)	CSF Volume (cm^3)	PBV	Total Memory	Motor Speed	Processing Speed	Total Mood	NPZ-8	ADC Stage	HAART
1	40	F	16	323,000	974.4	257.0	.791	37	6	9	306	12	0.5	−
2	45	M	324	56,200	1,251.8	348.0	.782	31	2	4	307	5	0.5	+
3	43	M	256	40,600	830.2	454.0	.646	31	4	0	271	3	0.5	+
4	56	M	563	ND	1,049.7	369.0	.740	41	5	3	296	5	0.5	+
5	44	M	321	<50	1,094.7	266.4	.804	39	2	0	306	2	0.5	+
6	45	M	190	<20	1,605.4	264.5	.858	32	1	7	344	6	1	+
7	45	M	818	ND	1,001.5	372.3	.729	31	5	8	259	8	1	+
8	33	M	355	<20	1,294.2	317.6	.803	63	0	0	240	0	0	+
9	40	M	465	<400	1,179.7	239.1	.831	31	0	4	282	3	0	+
10	37	M	519	<20	1,264.1	265.3	.826	44	0	0	215	0	0	+
11	39	M	87	20,800	1,211.8	329.9	.786	54	0	3	280	0	0	+
12	28	F	108	15,524	1,009.2	134.5	.882	ND	ND	ND	ND	7	0	+
13	25	M	190	155,613	1,228.8	153.4	.889	49	1	1	264	3	0	+
14	30	F	573	<50	1,118.7	101.7	.917	33	0	0	288	0	0	+
15	38	M	1,032	<20	1,342.2	174.4	.885	25	0	0	283	0	0	+
16	36	F			1,112.4	142.9	.886	60	0	0	292	0	0	−
17	22	M			1,093.1	218.9	.833	47	0	0	243	0	0	−
18	35	F			1,155.5	203.6	.851	56	0	1	255	1	0	−
19	45	F			1,089.4	125.7	.897	38	0	0	244	0	0	−
20	45	M			1,228.4	134.8	.901	35	0	2	294	0	0	−

Note.—CD4 indicates cluster of differentiation 4; PBV, percentage of parenchymal brain volume; ADC, AIDS dementia complex; HAART, highly active antiretroviral therapy; ND, no data.

TABLE 2: Correlations between percentage of PBV and behavioral measures

Behavioral Measure	Correlation	*P* Value
AIDS dementia complex*	−0.64	<.001
NPZ-8*	−0.50	<.05
Motor speed impairment*	−0.69	<.001
Processing speed impairment	−0.38	NS
Total memory impairment†	0.12	NS
Total mood dysfunction*	0.02	NS

Note.—NS indicates not significant at the $P = .05$ level.

* Spearman rank order correlation.

† Pearson product moment correlation.

Discussion

Although brain atrophy is usually found in patients with ADC, the relationship of brain atrophy to neurocognitive function, to stage of infection, and to immune status has been largely undefined. ADC is associated with HIV-1 infection of macrophages and microglia in the CNS and the release of neurotoxins that ultimately induce parenchymal damage, including significant neuronal loss and brain atrophy. The major pathologic features of ADC are cortical atrophy with varying degrees of dropout (≤50%) of cortical pyramidal neurons, altered cortical neuronal dendritic spine density and morphology, myelin pallor, and astrocytic proliferation (25–30). Milder forms of neurocognitive impairment may precede ADC. In general, the clinical manifestations of ADC occur in later stages of AIDS when plasma HIV RNA load increases and cluster of differentiation 4 counts decrease, and they are linked to release of neurotoxic metabolites and cytokines by infected macrophages and microglia within the brain parenchyma. Ultimately, ADC patients show dramatic loss of brain volume along with progressive deficits in psychomotor function and cognition. With more effective suppression of HIV-1 replication through the use of highly active anti-retroviral therapy, the risk of development of neurocognitive dysfunction may be decreased (31, 32), although it remains unclear how highly active anti-retroviral therapy affects the natural history of CNS HIV-1 infection and the resulting neurodegeneration and brain atrophy.

Most published neuroradiographic studies of ADC offer only qualitative assessments of atrophy. Poutianen et al (33), in 1992, used qualitative visual assessment of MR images to qualitatively describe the presence or absence of brain atrophy and to show associations between memory function and brain volume loss in HIV-1 infection. Quantitative studies of brain atrophy have often been limited to gross morphometric measures of linear dimensions in one or more axial planes that suffer from high inter- and intraobserver variability (34–39). Recently, several groups have attempted to implement more reliable techniques using segmentation analysis (classification of image pixels into specific tissue classes such as parenchyma, CSF, and others) rather than linear tracing to estimate brain volumes (40, 41). Paley et al (40), in 1994, used an automated segmentation tech-

nique to measure the CSF-to–intracranial volume ratio in 69 control participants and 189 HIV-infected patients and found that the CSF-to–intracranial volume ratio is significantly increased in symptomatic patients with late stage AIDS. These authors concluded that brain atrophy is a late stage phenomenon in ADC. In contrast, Jernigan et al (35), in 1993, estimated gray matter and white matter brain volumes using a manual stereotactic tracing technique in a total of 66 HIV-1 seropositive men, 31 of whom had non-neurologic symptoms and 35 of whom were asymptomatic. Control groups included a high-risk seronegativecohort and a cohort of seronegative patients with various psychiatric illnesses. Interestingly, the symptomatic patients (none with ADC) and some of the high-risk seronegative participants showed reduced volumes of cerebral gray matter and white matter and increased CSF volume. Some of the volume loss in the high-risk seronegative group was attributed to drug and alcohol use. Nonetheless, this study showed brain volume loss in HIV-1 infection even without overt neurologic dysfunction. Whether these patients were at increased risk for development of ADC was not determined.

Published studies to date indicate that brain atrophy results from HIV-1 infection in the CNS; that although atrophy may predominate in subcortical structures, it is a diffuse process affecting both gray and white matter; and that atrophy is generally more pronounced in neurologically impaired patients. However, the natural history of brain parenchymal loss and associated neurocognitive dysfunction during the course of HIV infection is unknown. Furthermore, techniques previously used for analysis of brain parenchymal volume in a number of studies generally suffer from high inter- and intraobserver variability and low sensitivity. Unanswered questions include whether development of brain atrophy begins early after infection or whether it develops later, after significant immunosuppression, and whether brain atrophy is a sensitive, objective early marker for future neurocognitive dysfunction. Notably, concurrent opportunistic CNS infections, such as cytomegalovirus and toxoplasmosis, may also contribute to development of brain atrophy in cases of AIDS (42), although our patients were free of such infections.

To more fully understand the natural history of neurodegeneration in patients with HIV-associated neurocognitive dysfunction, we used a highly reproducible, validated image processing methodology for the assessment of brain PBV. With PBV, this article differs from previous reports in several ways. Our technique uses 3-mm contiguous sections, whereas several past studies have used ≥5-mm-thick sections (34, 36, 40, 43–45), which were noncontiguous in several studies (35, 38, 46, 47). Because HIV diffusely affects the brain, we performed whole-brain volume measurements, whereas many past studies used regional volume measurements (34–36, 43–47). This image processing technique is not affected by high inter- and intraobserver variability, as several past studies (34–39) have been.

Our results provide support to the theory that HIV infection ultimately diffusely affects the entire brain parenchyma and that brain atrophy occurs in HIV-infected patients even in the absence of overt clinical dysfunction manifested as ADC (36). Furthermore, our showing a significant correlation between subtest scores of motor impairment and PBV is consistent with the early development of atrophy in the basal ganglia in cases of HIV infection in the CNS and early development of motor impairment (44). Multiple pathologic studies describing neuronal loss within the basal ganglia as well as in the brain cortex in HIV-positive patients support this assertion (48–54), as do MR spectroscopy studies that show significant (*N*-acetylaspartate) NAA reductions in patients with HIV, a quantitative indicator of neuronal degeneration (55).

We found that neurocognitive deficits (higher NPZ-8 and clinical ADC staging scores) were significantly correlated with brain atrophy (lower brain volume). This suggests that PBV loss in general may predict poor neuropsychological test performance as well as more clinically apparent neurologic dysfunction (ADC stage score). Furthermore, our studies show that HIV infection itself is significantly correlated with poor neuropsychological performance. In total, these data indicate that HIV infection puts a person at risk for neuropsychological impairment (as defined by both neuropsychological test performance and clinical dysfunction manifested as ADC) as well as PBV loss. This suggests a quantifiable and clinically significant link between HIV infection and brain atrophy, as measured by PBV. We speculate that quantitation of PBV changes in HIV-infected persons over time may offer a means of identifying patients at increased risk for dementia and may offer a means of determining the neuroprotective potential within the CNS of anti-HIV drug regimens.

We have not attempted to correlate cluster of differentiation 4 count, concomitant use of antiretroviral drugs, or plasma RNA level with the PBV in this patient cohort, because our study represents a cross-sectional examination at a single time point in the course of HIV-1 infection. Published data suggest that cluster of differentiation 4 counts do not correlate with an increased risk for AIDS dementia (10), and although a high plasma viral load is observed in some patients with AIDS dementia (56), this is not a consistent finding (57). Correlations of these parameters with PBV requires a much larger patient cohort with longitudinal analysis. Because both cluster of differentiation 4 count and plasma RNA levels often change dramatically with changes in anti-retroviral therapy, we think that single-point, cross-sectional paraclinical markers such as cluster of differentiation 4 count and viral load are not reliable correlates for PBV, which reflects a chronic neurodegenerative process. Quantitation of PBV, however, offers a reliable measure of cumulative effects of HIV-1 infection in the CNS, without the confounding problem of short-term fluctuations, and it may provide a useful means for longitudinal follow-up of patients who are at risk for the development of neurocognitive dysfunction.

Conclusion

We have shown that neurocognitive deficits (higher NPZ-8 and clinical ADC staging scores) are significantly correlated with brain atrophy (lower PBV) in a cohort of HIV-infected and noninfected persons. This suggests that PBV loss in general may predict poor neuropsychological test performance as well as more clinically apparent neurologic dysfunction (ADC stage score). Specific tests of motor function may provide a rapid screen for patients who are at risk of PBV loss. Furthermore, our studies show that HIV infection itself is significantly correlated with poor neuropsychological performance. In total, these data indicate that HIV infection puts a person at risk for neuropsychological impairment (as defined by both neuropsychological test performance and clinical dysfunction manifested as ADC or specific motor impairment) and PBV loss. This suggests a quantifiable and clinically significant link between HIV infection and brain atrophy, as measured by PBV. We speculate that quantitation of PBV changes in HIV-infected persons over time may offer a means of identifying patients who are at increased risk for the development of dementia and may offer a means of determining the neuroprotective potential within the CNS of anti-HIV drug regimens.

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