Reversal of Brain Metabolic Abnormalities Following Treatment of AIDS Dementia Complex with 3′-azido-2′,3′-Dideoxythymidine (AZT, Zidovudine): A PET-FDG Study

Arturo Brunetti*, Gary Berg, Giovanni Di Chiro, Robert M. Cohen, Robert Yarchoan, Philip A. Pizzo, Samuel Broder, Janie Eddy, Michael J. Fulham, Ronald D. Finn, and Steven M. Larson†

Neuroimaging Section, NINCDS; Nuclear Medicine Department and Clinical Brain Imaging Section, NIMH; Division of Cancer Treatment and Pediatric Branch NCI; and National Institutes of Health, Bethesda, Maryland

Brain glucose metabolism was evaluated in four patients with acquired immunodeficiency syndrome (AIDS) dementia complex using [^{18}F]fluorodeoxyglucose (FDG) and positron emission tomography (PET) scans at the beginning of therapy with 3′-azido-2′,3′-dideoxythymidine (AZT, zidovudine), and later in the course of therapy. In two patients, baseline, large focal cortical abnormalities of glucose utilization were reversed during the course of therapy. In the other two patients, the initial PET study did not reveal pronounced focal alterations, while the post-treatment scans showed markedly increased cortical glucose metabolism. The improved cortical glucose utilization was accompanied in all patients by immunologic and neurologic improvement. PET-FDG studies can detect cortical metabolic abnormalities associated with AIDS dementia complex, and may be used to monitor the metabolic improvement in response to AZT treatment.

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Severe cognitive, behavioral, and motor abnormalities occur frequently in patients with acquired immunodeficiency syndrome (AIDS) in the absence of opportunistic infections or tumors of brain. This condition, which is associated with pathologic abnormalities primarily involving the white matter, is known as AIDS dementia complex (*1–4*). It usually appears late in the course of AIDS and, characteristically, once symptoms have been established, there is rapid progression of the disease in the absence of treatment (*1*). However, cognitive dysfunction attributable to human immunodeficiency virus-1 (HIV-1) can occur early in the course of the disease and can be rather subtle. In particular, symptoms may occur earlier in children (*2,3*) and some impairment appears to affect nearly all patients (*3*). 3′-azido-2′,3′-dideoxythymidine (AZT, zidovudine) has been reported to be successful in the treatment of AIDS and AIDS dementia complex (*5–8*). In a preliminary report (*7*) we noted that one patient with AIDS dementia complex had a normalization of the pattern of cerebral glucose utilization upon imaging with positron emission tomography (PET) and fluorine-18 fluorodeoxyglucose ([^{18}F]FDG). In the present study, we report the PET-FDG studies of this and three additional patients with AIDS dementia complex at the beginning and in the course of AZT treatment.

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For reprints contact: Giovanni Di Chiro, MD, Neuroimaging Section, NINCDS, NIH, Bldg. 10, Rm.1C451, Bethesda, MD 20892.

*Present address: Medicina Nucleare-Istituto di Scienze Radiologiche, 2nd Medical School, Naples, Italy.

† Present address: Nuclear Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY.

MATERIALS AND METHODS

Patients

Four patients with AIDS dementia complex were studied (three male homosexuals, ages 32, 32, and 35 yr, and an 11-yr-old boy with hemophilia). The patients were all treated

with AZT according to protocols of the National Cancer Institute. Informed consent for evaluation and PET studies were obtained from the patient or their guardians. In every case a thorough clinical, immunologic, and neurologic assessment was carried out prior to and during AZT therapy. A series of neuropsychologic tests was used to assess intellectual ability, memory, motor performance, attention, and orientation in the three adult patients. Intellectual ability, verbal performance, and development were evaluated in the 11-yr-old boy. The results of the psychometric tests have been previously reported (*6–8*).

PET Studies

PET studies were performed 45 min after i.v. administration of 5 mCi (185 MBq) FDG in the three adult patients and 2.5 mCi (93 MBq) FDG in the pediatric patient. Timed arterial blood samples were obtained from the radial artery in the three adult patients. Timed venous blood samples were obtained from a central venous catheter in the 11-yr-old boy. During the interval between the administration of FDG and the PET scan the patients were kept at rest in a darkened room, but eye patches and ear plugs were not used. PET studies were performed with a Scanditronix PC-1024 multislice scanner (5 mm in plane resolution, 11-mm-slice thickness, and 13-slice separation). The attenuation correction was performed in two patients with transmission scans, while in the other two patients it was calculated from an elliptical outline with an automated routine. Glucose metabolic rates (GMR) were calculated according to the Sokoloff model (*9*), using the simplified operational equation derived by Brooks (*10*).

Image Analysis

All PET images were first visually analyzed, in search of focal areas of relatively increased or decreased glucose utilization. Quantitative image analysis of cortical metabolism was performed on five standardly selected supratentorial planes (*11*). Regional glucose metabolic rates of cerebral cortex were determined with a standard series of 61 ROIs (Fig. 1). Mean cortical GMRs were calculated from the regional metabolic rates. Regional "scores" were subsequently obtained by dividing in each study the regional metabolic rates by the mean cortical GMR. This normalization procedure was performed in order to obtain a quantitative evaluation of regional metabolic patterns, not dependent on absolute metabolic rate values. Regional scores in the AIDS patients were compared with average regional scores determined in the group of ten normal volunteers (Table 1). Mean normal scores ± 3 s.d. were used as a cutoff level for definition of hyper- and hypometabolic regions.

RESULTS

Case Reports

Patient 1. A 32-yr-old homosexual male with human immunodeficiency virus-1 (HIV-1) infection diagnosed in February 1985, was referred to the National Institutes of Health (NIH) in July 1986 after a period of progressive mental deterioration. The neurologic examination showed weakness of the extremities, with wide-based gait. Nerve conduction studies and EMG showed a pattern consistent with sensori-motor neuropathy. The psychometric evaluation revealed abnormal memory, visual-spatial perception, and motor performance with globally impaired mental ability. A post-contrast computed tomography (CT) scan showed moderate, generalized, ventricular and sulcal dilatation, and peri-ventricular white matter hypodensity. The patient was diagnosed as having AIDS dementia complex. He was started on AZT (zidovudine), 250 mg every 4 hr per os. The baseline PET-FDG study, performed during the second week of treatment, showed an abnormal pattern of cortical glucose utilization, with relatively increased frontal metabolism, and relatively decreased temporo-occipital metabolism (Table 2). The quantitative ROI analysis revealed three hypermetabolic frontal regions (A2, D3, D4), one hypermetabolic midline parietal region (A8), two symmetric hypometabolic temporal regions (D6, D7), and two hypometabolic occipital regions (C14, D12) (see Table 1).

Regional metabolic asymmetries were no longer seen in the repeat PET-FDG study, 10 wk after the beginning of treatment (Table 2). The quantitative analysis of

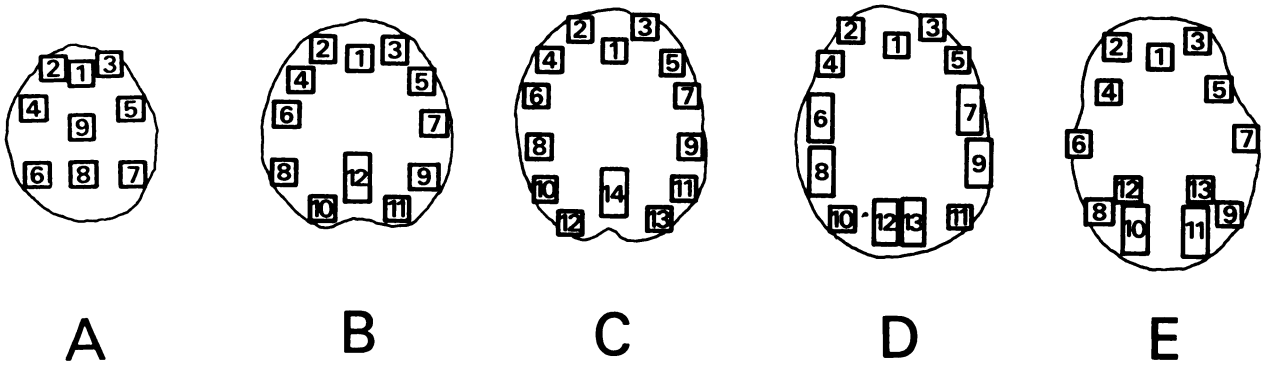

FIGURE 1
Regions of interest used to evaluate cortical glucose metabolism in five standardly selected planes 13 mm apart. Plane E, the most caudal, is 4 cm above the infra-orbito-meatal plane. Right side of figure corresponds to patient's right side in this and in the following figures.

TABLE 1
Regional Scores for Normal Controls and Patients for Plane D

Controls	Regions of interest												
Age/race/sex	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D12	D13
1 26 white M	0.93	0.93	0.94	1.03	1.09	1.00	0.93	1.04	0.94	0.96	0.92	0.83	0.83
2 43 white F	0.86	0.85	0.89	1.14	0.90	1.07	1.00	1.00	0.94	0.71	0.69	0.97	0.88
3 29 white M	0.99	0.96	0.88	1.06	0.97	1.09	0.95	0.95	0.82	0.81	0.82	0.90	0.88
4 29 white M	0.86	0.87	1.02	1.00	1.03	1.10	1.02	0.91	0.88	0.78	0.79	1.04	1.01
5 58 white F	0.87	0.90	0.93	0.94	0.95	1.02	1.14	0.97	0.97	0.78	0.80	0.99	0.98
6 20 white M	0.99	0.88	0.89	1.02	1.08	1.02	1.04	0.73	0.83	0.94	0.83	0.65	0.58
7 55 white M	0.96	0.77	0.84	0.96	0.95	0.98	1.01	1.03	1.00	0.76	0.85	1.04	1.00
8 62 white M	0.94	0.94	0.89	0.96	1.04	1.05	1.07	0.98	0.96	0.79	0.79	1.12	1.07
9 47 white M	1.12	0.98	0.97	1.05	1.11	1.05	1.13	0.97	0.94	0.77	0.78	0.97	1.03
10 62 white M	0.92	0.88	0.85	1.02	0.99	1.01	0.97	0.98	0.97	0.89	0.89	1.12	1.12
Mean ± 3 s.d.'s	0.94 ± 0.24	0.90 ± 0.18	0.91 ± 0.18	1.02 ± 0.18	1.01 ± 0.21	1.04 ± 0.12	1.03 ± 0.21	0.96 ± 0.27	0.93 ± 0.18	0.79 ± 0.27	0.79 ± 0.20	0.99 ± 0.27	0.96 ± 0.20

Patients	Regions of interest												
A—Pre-AZT B—Post-AZT	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D12	D13
1 32 white M													
A	1.15	1.11	1.20	1.24	1.15	0.90	0.82	0.88	0.90	0.73	0.76	0.68	0.77
B	0.95	0.92	0.94	1.00	0.97	0.95	0.97	0.84	0.96	0.80	0.85	0.84	0.99
2 32 white M													
A	0.87	0.91	0.88	1.03	0.99	1.07	1.00	0.98	0.90	0.87	0.83	0.97	0.94
B	0.97	0.97	0.93	1.00	1.01	0.96	1.01	0.95	0.97	0.78	0.72	0.96	0.87
3 35 white M													
A	1.01	0.91	1.04	1.00	0.98	0.88	0.96	0.88	0.91	0.96	1.03	1.02	1.04
B	1.07	0.92	1.02	1.00	1.03	0.88	0.87	0.86	0.87	0.85	0.88	1.13	1.16
4 11 white M													
A	0.70	0.92	0.65	0.92	0.77	0.88	0.74	1.08	0.86	0.98	0.78	1.10	1.14
B	0.93	0.96	0.94	1.04	0.97	0.93	0.88	0.96	0.89	0.89	0.85	0.94	0.97
Mean ± 1 s.d.													
A	0.93 ± 0.19	0.96 ± 0.10	0.94 ± 0.23	1.04 ± 0.14	0.97 ± 0.16	0.93 ± 0.09	0.88 ± 0.12	0.92 ± 0.10	0.89 ± 0.02	0.89 ± 0.04	0.85 ± 0.12	0.94 ± 0.18	0.97 ± 0.16
B	0.98 ± 0.06	0.94 ± 0.03	0.95 ± 0.04	1.01 ± 0.02	0.99 ± 0.03	0.93 ± 0.04	0.93 ± 0.07	0.90 ± 0.06	0.92 ± 0.05	0.83 ± 0.05	0.83 ± 0.07	0.96 ± 0.12	0.99 ± 0.12

* Mean cortical GMR (n = 10) = 7.55 ± 0.98 (mean ± 1s.d.) mg glucose/100 g tissue/min; cortical GMR of AIDS patients are reported in Table 2.

TABLE 2
Summary of CT/MR and PET Findings in Four Patients with AIDS Dementia Complex

Patient no.	Age (yr)/sex	Baseline CT/MR	Repeat CT/MR	Baseline PET study	Repeat PET study
1	32/M	Moderate, generalized brain atrophy and periventricular white matter hypodensity.	Unchanged	Bilateral temporo-occipital hypometabolism and frontal hypermetabolism. mean cGMR = 7.95*	Cortical metabolic asymmetries no longer evident. mean cGMR = 5.95
2	32/M	Mild brain atrophy. Focal symmetrical hyperintense areas in each centrum semiovale, in T_2-weighted images.	Unchanged	Mildly abnormal cortical metabolic pattern. mean cGMR = 8.43	Generalized increase of cortical GMR, and normal cortical metabolic pattern. mean cGMR = 11.01
3	35/M	Mild brain atrophy and periventricular white matter hypodensity.	Unchanged	Generalized, low cortical glucose metabolism. mean cGMR = 4.74	Marked, generalized increase of cortical glucose metabolism. mean cGMR = 8.53
4	11/M	Moderate brain atrophy and some white matter hypodensity more evident around the right frontal horn.	Regression of white matter hypodensity.	Right fronto-temporal and left cerebellar hypometabolism. mean cGMR = 7.10	Normalization of cortical metabolic pattern. Persistent left cerebellar hypometabolism. mean cGMR = 9.59

Mean cGMR = mean cortical glucose metabolic rate (mg glucose/100 g tissue/min).
* Baseline PET study in patient 1 was obtained during the second week of treatment.

regional cortical glucose utilization revealed no abnormal scores in the repeat PET-FDG study. Concomitantly, the patient's mental and neurologic conditions improved dramatically. His memory, attention, and movement coordination improved. His muscle strength and his gait also improved, and the patient resumed walking long distances unassisted. A repeat CT scan showed no significant change compared to pre-treatment. The patient's mental condition remained stable for the next 3 mo of treatment. The dose of AZT was decreased in December 1986 because of severe thrombocytopenia, and he died 1 mo later from *Pneumocystis carinii* pneumonia. Autopsy showed minimal spongy changes in the medulla oblongata.

Patient 2. A 32-yr-old homosexual male with HIV-1 infection diagnosed in February 1986 was referred to the National Institutes of Health (NIH) in October 1986, after a 6-mo period of progressive mental deterioration, with memory loss associated with decreased writing ability and difficulties in concentrating. The neurologic examination showed decreased coordination, slowing of alternate movements, and generalized weakness. The psychometric assessment revealed abnormal visual-spatial perception, motor performance, and intellectual ability. Post-contrast CT scan showed mild brain atrophy, while magnetic resonance imaging (MRI) demonstrated two symmetric areas of increased signal intensity in each centrum semiovale in the T_2 weighted images (Fig. 2). A diagnosis of AIDS dementia complex was made, and the patient was started on AZT, 250 mg every 4 hr per os. PET-FDG studies were performed at the beginning and after 6 wk of treatment. The baseline PET-FDG study did not reveal marked focal cortical abnormalities (Fig. 3; upper row). The regional score analysis demonstrated one hypermetabolic frontal region (B3) and one hypometabolic frontal region (A2). The repeat PET study showed a 30.6% increase in mean cortical GMR compared to the baseline study (Fig. 3, lower row; Table 2). No abnormal scores were found in the repeat PET-FDG study. The patient's cognitive function improved substantially after being started on AZT treatment. Psychometric test scores were back to normal values and a neurologic examination showed normal coordination and speed of alternating movements after 2 mo of treatment. No changes were observed in the repeat CT and MRI scans, compared to pre-treatment. The patient's mental condition remained stable in the following 7 mo of treatment. However, he subsequently developed cryptococcal meningitis and expired.

Patient 3. A 35-yr-old homosexual male with HIV-1 infection diagnosed in May 1985, was referred to the NIH in November 1986 after a progressive deterioration of his mental ability. A post-contrast CT scan showed mild brain atrophy and periventricular white matter hypodensity, with no focal lesions (Fig. 4). The psychometric evaluation confirmed the diagnosis of AIDS dementia complex, and the patient was started on AZT, 250 mg every 4 hr per os. The baseline PET-FDG study showed low cortical GMR (Table 2). The regional score analysis revealed three hypometabolic regions (two frontal A2 and A3, and one left temporal D6). The repeat study after 2 mo of treatment demonstrated a 79.9% increase of the mean cortical GMR (Fig. 5, Table 2), with correspondent, marked, clinical improvement. Regions A2 and D6 were still hypometabolic in the post-treatment study, where also one hypermetabolic occipital region (C14) was found. During the first 2 mo of treatment the patient's alertness, memory and motor performance improved. The patient responded to AZT treatment in the next 15 mo. However, he subsequently developed HIV-1 associated cardiomyopathy, and expired.

Patient 4. An 11-yr-old hemophiliac boy, with HIV-1 infection diagnosed in 1984, was referred to NIH in February 1987. The neurologic examination showed a wide-based ataxic gait, weakness of the left ilio-psoas and quadriceps, with bilateral pyramidal signs. A psychometric evaluation revealed that he had lost 28 IQ points compared to school testing that had been done before he acquired HIV-1 disease. A postcontrast brain CT scan showed moderate brain atrophy and periventricular white matter hypodensity more marked around the right frontal horn. The pre-treatment PET-FDG study showed a markedly abnormal glucose utilization, with right front-temporal and left cerebellar hypome-

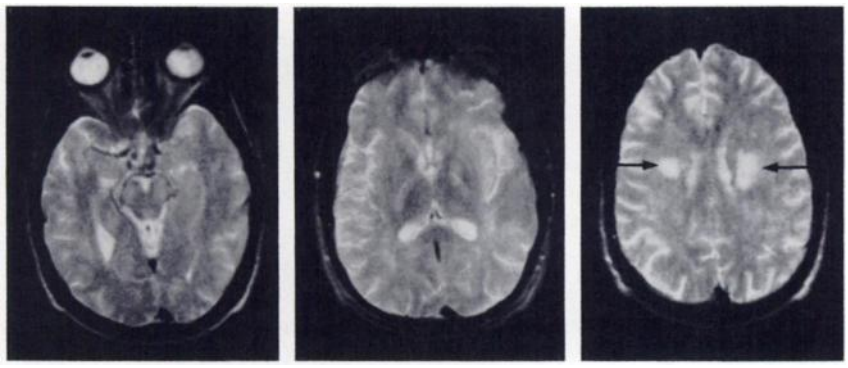

FIGURE 2
Patient 2. Pre-treatment T_2-weighted MR images (TR = 2,000 msec; TE = 80 msec) showing mild brain atrophy, and symmetric areas of increased signal intensity in each centrum semiovale (arrows). Postcontrast brain CT scans (not shown) demonstrated bilateral periventricular white matter hypodensity, but no focal lesion.

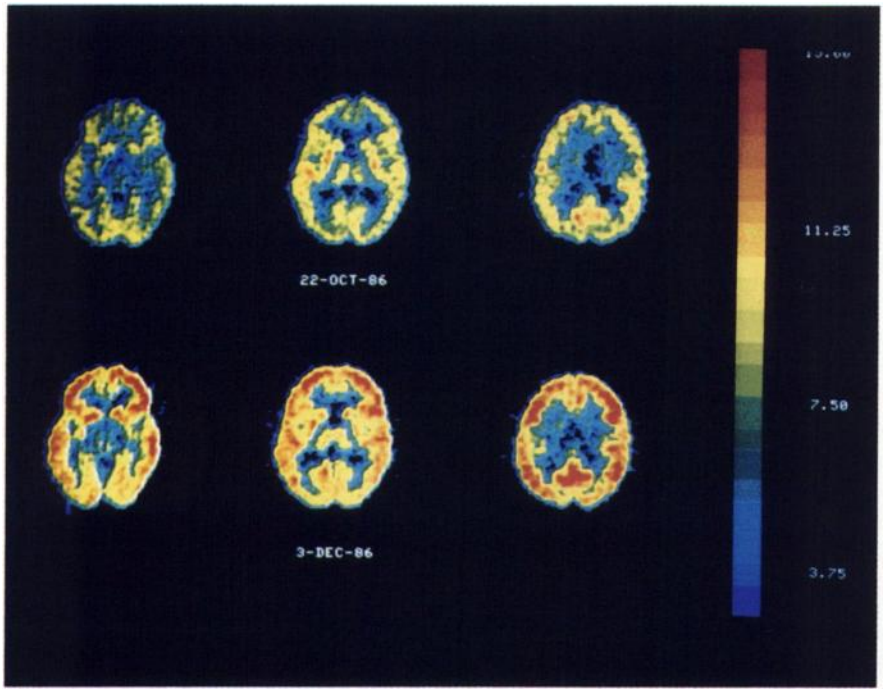

FIGURE 3
Patient 2. Baseline (upper row) and post-treatment (lower row) PET-FDG images (planes, E, D, and B from left to right). The post-treatment study showed a 30.6% increase in mean cortical GMR (Table 2). Color scale represents glucose metabolic rates (mg glucose/100g tissue/min) in this and in the following PET images.

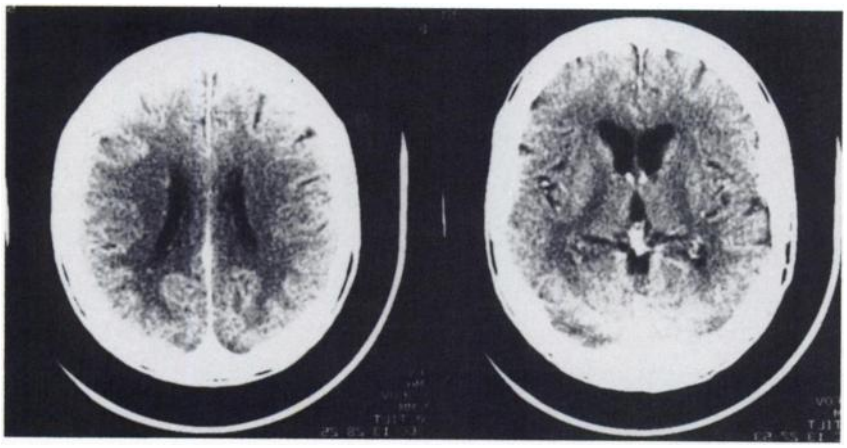

FIGURE 4
Patient 3. Postcontrast, pre-treatment brain CT scan showing mild brain atrophy and diffuse hypodensity of periventricular white matter, with absence of focal parenchymal lesions.

tabolism (Fig. 6A, Table 2). The baseline regional scores analysis revealed six abnormally hypometabolic regions, two midline frontal (B1, D1), two right frontal (D3, D5), one right temporal (D7), and one left temporal (D6). Two hypermetabolic regions, one left frontal (C6) and one left temporo-occipital (E8) were also observed in the initial study. The patient was started on a continuous infusion of AZT (0.5 mg/kg/hr). The repeat PET-FDG study, performed after 12 wk of treatment, demonstrated a normal cortical glucose utilization (Fig. 6B) with persistent left cerebellar hypometabolism. In the post-treatment study only two abnormal regional scores were observed (D6, left temporal, still hypometabolic, and E9, right temporo-occipital, hyper-

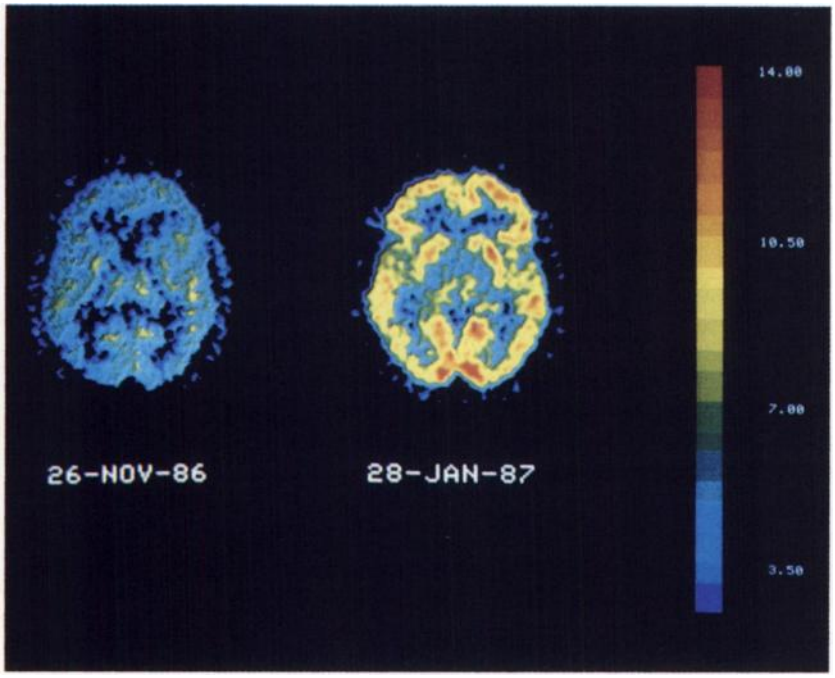

FIGURE 5
Patient 3. Pre-treatment (left) and post-treatment (right) PET-FDG images (plane D). Low glucose utilization was observed in the pre-treatment scan. The post-treatment study showed a 79.9% increase in mean cortical GMR. (Table 2).

metabolic). At the time of the repeat PET-FDG study, the mental status had significantly improved, while neurological signs persisted. Control brain CT scans showed disappearance of the white matter hypodensity. The patient's mental status improved continuously and his IQ returned to his pre-illness level at 9 mo of continuous AZT infusion therapy.

DISCUSSION

The neurotropism of human immunodeficiency virus-1 (HIV-1) is a critical factor in the clinical course of AIDS. HIV-1 is transported across the brain capillary barrier by infected macrophages (*12*) and can subsequently be found in glial and, rarely, neuronal cells (*13–15*). In fact, the nervous and the immune system share several cell surface receptors including CD4+, responsible for HIV-1 binding to helper/inducer lymphocytes (*16,17*). The pathogenetic mechanism of AIDS related neurologic disorders have not yet been elucidated (*3,4,6*). AZT (zidovudine) can effectively inhibit HIV-1 replication (*18*) and can penetrate into CSF (*19*). In addition, AZT has been shown to effectively inhibit HIV-1 replication in monocyte/macrophages (*20*). These observations suggest that AZT may reduce HIV-1 replication in the brain and provide a rationale for its use in the treatment of AIDS-related neurologic and psychiatric abnormalities (*5–8*).

PET-FDG studies can detect brain metabolic abnormalities in different forms of dementia (*21–25*). Brain metabolic abnormalities were also demonstrated in patients with AIDS dementia complex by Rottenberg et al. (*26*). Early relative subcortical hypermetabolism and progressive cortical and subcortical hypometabolism were found to be characteristic of this group of patients. Since AZT can reverse AIDS related neurologic and psychiatric abnormalities (*5–8*), we designed a feasibility trial for the evaluation of possible brain metabolic changes in patients with AIDS dementia complex in the course of AZT treatment.

In regard to the effect of treatment two patterns were observed in the four patients. In two cases (Patients 2 and 3) the baseline study revealed minor focal abnormalities of cortical glucose utilization, followed by marked increase (30.6% and 79.9%, respectively) in mean cortical GMR in the repeat study. In the other two patients (1 and 4), the baseline study revealed marked regional abnormalities of cortical glucose utilization. These focal abnormalities were no longer evi-

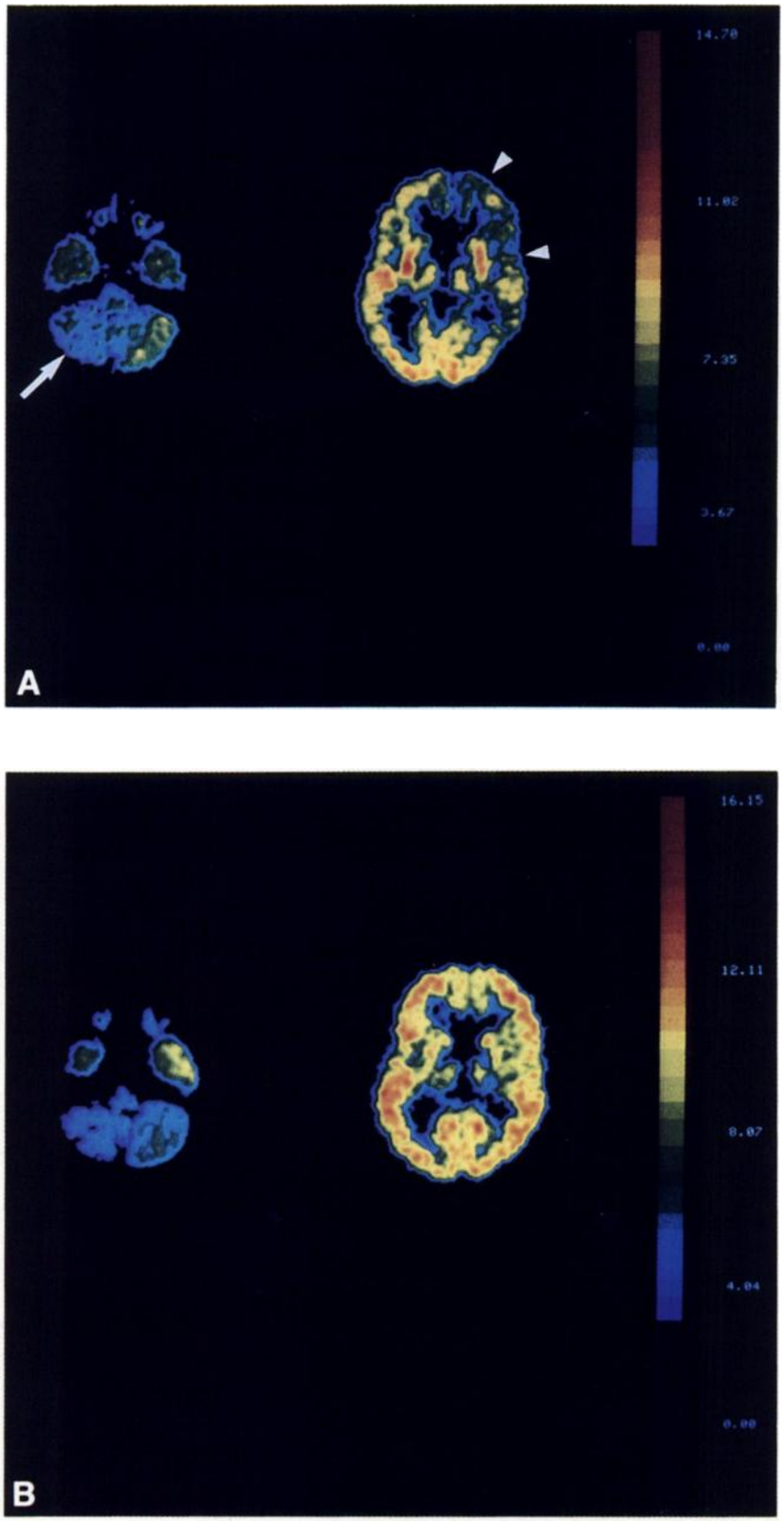

FIGURE 6
Patient 4. Pre-treatment (Fig. 6A) and post-treatment (Fig. 6B) PET-FDG images at the level of the cerebellum (left) and the basal ganglia (right). A: Baseline PET study shows left cerebellar (arrow) and right front-temporal (arrowheads) hypometabolism. B: Repeat PET study shows a normal cortical metabolic pattern, with persistent left cerebellar hypometabolism.

dent in the post-treatment PET-FDG study. Mean cortical GMR was decreased in Patient 1 (25.1%) and increased in Patient 4 (35.1%), compared with their baseline study. These GMR changes are significantly larger than those observed by other authors in PET-FDG studies repeated with a short time interval (*27–29*), and than those observed in six patients with affective disorders studied over 4–5 wk time intervals in our PET facility using the same equipment (mean change = 9.0%; Cohen RM: personal communication).

In conclusion, while in three patients we observed an increased cortical GMR in the repeat PET-FDG study, in Patient 1 cortical GMR was decreased in the repeat study. However, marked regional asymmetries observed in Patient 1's baseline study were completely reversed in the repeat study. We must note that the baseline study in Patient 1 was obtained after 2 wk of AZT treatment. In this regard, Patient 1 is different from the other three patients. AZT treatment is associated with rapid clinical and mental improvement in some patients and our "baseline" study might have been already affected by treatment. Furthermore the patient's mental condition was persistently improved throughout the period of treatment. We believe that in the case of Patient 1 the regression of the marked regional asymmetries of cortical glucose utilization, even if associated with decreased cortical GMR, could represent a substantial improvement of his brain metabolic function, in agreement with his dramatic clinical and mental improvement.

Regional metabolic abnormalities were detected by regional "score" analysis not dependent on absolute GMR values. Regional abnormalities were demonstrated at the time when patients had their most serious defects in mentation and neurologic function. Regional "score" analysis also revealed the normalization of regional glucose utilization with concomitant clinical and particularly mental improvement following treatment. However, no similar regional metabolic patterns were observed in the four patients. Both hypo- and hypermetabolic regional "scores" were demonstrated in the AIDS patients. Regional cortical hypometabolism could reflect functional deafferentation due to white matter disease. Regional hypermetabolism may depend on different causes, including cognitive and emotional factors. Frontal hypermetabolism in Patient 1's baseline study may reflect a condition of increased anxiety and attention (*11,30*). The hypermetabolic occipital score (C14) in Patient 3's repeat study could depend on minimal visual stimulation during FDG uptake. Functional activation of a left precentral area (C6) in the pediatric patient's baseline study could reflect movements of the right arm during FDG uptake. Interpretation of hypermetabolic scores can be difficult in the associative cortical areas, such as the hypermetabolic temporo-occipital regions (E8, E9) observed in the pediatric patient's baseline and repeat study.

Pathologic abnormalities in AIDS dementia complex have been predominantly found in white matter, and to a minor extent in subcortical gray matter, with relative sparing of the cortex (*31*). Basal ganglia GMR did not change significantly in Patient 1's repeat study, where basal ganglia were visually more prominent because of decreased cortical GMR. In the other three patients basal ganglia GMR increased to a minor extent compared to cortical GMR following AZT treatment. CT and MRI brain scans usually reveal a variable degree of brain atrophy in patients with AIDS dementia complex. White matter involvement is also frequently observed in these patients, in the form of hypodense areas with CT, and hyperintense areas in T_2-weighted MRI images (*32,33*). PET-FDG studies allowed us to detect cortical functional changes in the absence of correspondent CT and MRI documented cortical changes. Cortical metabolic abnormalities could in part reflect white matter involvement. However, the possibility of a direct or indirect viral action on cortical gray matter has to be considered. For example, sequence homologies have been described between the HIV-1 envelope protein gp120 and peptides acting as neurotransmitters (*16*), and a neuroactive factor called neuroleukin (*34*). HIV-1 produced gp120 could then interfere with binding of these proteins to nervous tissue, with subsequent metabolic alterations.

SUMMARY

PET-FDG studies suggest that functional brain impairment in AIDS dementia complex can be accompanied by regional or generalized alterations of glucose metabolism, and that effective anti-viral therapy can reverse these metabolic abnormalities. Imaging with PET may offer diagnostic information and may suggest insights into the pathophysiology of the symptoms observed in AIDS dementia complex. Abnormalities shown on CT and MRI tend to reflect brain atrophy and white matter involvement which do not generally change in parallel with the clinical improvement related to AZT treatment. AIDS dementia complex is an at least partially reversible type of dementia.

PET-FDG studies may be clinically useful in detecting global and regional brain metabolic abnormalities associated with AIDS dementia complex, and may assist in monitoring the response to anti-viral treatment.

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REFERENCES

1. Navia BA, Jordan BD, Price RW. The AIDS dementia complex: I. clinical features. *Ann Neurol* 1986; 19:517–524.
2. Epstein LG, Sharer LR, Oleske JM, et al. Neurologic manifestations of human immunodeficiency virus infection in children. *Pediatrics* 1986; 78:678–687.
3. Price RW, Brew B, Sidtis J, Rosenblum M, Sheck AC, Cleary P. The brain in AIDS: central nervous system HIV-1 infection and AIDS dementia complex. *Science* 1988; 239:586–591.
4. Brunet P, Bolgert F, Pierrot-Deseilligny C. L'infection du systeme nerveux par le virus du deficit immunitaire humain acquis. *Rev Neurol* 1988; 144:317–326.
5. Yarchoan R, Broder S. Development of antiretroviral therapy for acquired immunodeficiency syndrome and related disorders: a progress report. *N Engl J Med* 1987; 316:557–564.
6. Yarchoan R, Thomas RV, Grafman J, et al. Long term administration of 3′-azido-2′,3′-dideoxythymidine to patients with AIDS related neurological disease. *Ann Neurol* 1988; 23 (suppl):S82–S87.
7. Yarchoan R, Berg G, Browers P, et al. Response of human immunodeficiency virus-associated neurological disease to 3′-azido-3′-deoxythymidine. *Lancet* 1987; 1:132–135.
8. Pizzo PA, Eddy J, Falloon J, et al. Effect of continuous intravenous infusion of zidovudine (AZT) in children with symptomatic HIV infection. *N Engl J Med* 1988, V319:889–896.
9. Sokoloff L, Reivich M, Kennedy C, et al. The (^{14}C)deoxyglucose method for the measurement of local cerebral glucose utilization: theory, procedures and normal values in the conscious and anesthetized albino rat. *J Neurochem* 1977; 28:897–916.
10. Brooks RA. Alternative formula for glucose utilization using labeled deoxyglucose. *J Nucl Med* 1982; 23:538–539.
11. Cohen RM, Semple WE, Gross M, et al. Dysfunction in a prefrontal substrate of sustained attention in schizophrenia. *Life Sic* 1987; 40:2031–2039.
12. Gartner S, Markovitz P, Markovitz DM, et al. The role of mononuclear phagocytes in HTLV-III/LAV infection. *Science* 1986; 233:215–219.
13. Wiley CA, Schreier RD, Nelson JA, Lampert PW, Oldstone MB. Cellular localization of human immunodeficiency virus infection within the brains of acquired immunodeficiency syndrome patients. *Proc Natl Acad Sc USA* 1986; 83:7089–7093.
14. Stoler MH, Eskin TA, Benn S, Angerer RC, Angerer LM. Human T-cell lymphotropic virus type III infection of the central nervous system. *JAMA* 1986; 256:2360–2364.
15. Gyorkey F, Melnick JL, Giorkey P. Human immunodeficiency virus in brain biopsies of patients with AIDS and progressive encephalopathy. *J Infect Dis* 1987; 155:870–876.
16. Pert CB, Hill JM, Ruff MR, et al. Octapeptides deduced from the neuroreceptor-like pattern of antigen T-4 in brain potently inhibit human immunodeficiency virus receptor binding and T-cell infectivity. *Proc Natl Acad Sci USA* 1986; 83:9254–9258.
17. Hill JM, Farrar WL, Pert CB. Autoradiographic localization of T4 antigen, the HIV receptor, in human brain. *Intern J Neurosci* 1987; 32:687–693.
18. Mitsuya H, Weinhold KJ, Furman PA, et al. 3′-azido-3′-deoxythymidine (BWA509U): an antiviral agent that inhibits the infectivity and cytopathic effect of human T-lymphotropic virus in vitro. *Proc Natl Acad Sc USA* 1985; 82:7096–7100.
19. Klecker LW, Collins JM, Yarchoan R, et al. Plasma and cerebrospinal fluid pharmacokinetics of 3′-azido-3′-deoxythymidine: a novel pyrimidine analog with potential application for the treatment of patients with AIDS and related diseases. *Clin Pharmacol Ther* 1987; 41:407–412.
20. Perno CF, Yarchoan R, Cooney DA, et al. Inhibition of human immunodeficiency virus (HIV-1/HTLV-III$_{Ba-L}$) replication in fresh and cultured human peripheral blood monocyte/macrophages by AZT and related 2′,3′-dideoxynucleosides. *J Exp Med* 1988: in press.
21. Friedland RP, Budinger TF, Ganz E, et al. Regional cerebral metabolic alterations in dementia of the Alzheimer type: Positron Emission Tomography with (^{18}F)fluorodeoxyglucose. *J Comput Assist Tomogr* 1983; 7:590–598.
22. Kuhl DE, Metter EJ, Riege WH, et al. Local cerebral glucose utilization in elderly patients with depression, multiple infarct dementia and Alzheimer's disease. *J Cereb Blood Flow Metab* 1983; 3(suppl 1): S494–495.
23. Kuhl DE, Metter EJ, Riege WH, Markham CH. Patterns of cerebral glucose utilization in Parkinson's disease and Huntington disease. *Ann Neurol* 1984; 15(suppl 3):S119–S125.
24. Chase TN, Foster LN, Fedio P, Brooks RA, Mansi L, Di Chiro G. Regional cortical dysfunction in Alzheimer's disease as determined by positron emission tomography. *Ann Neurol* 1984; 15(suppl 3):S170–174.
25. Berg G, Grady CL, Sundaram M, et al. Positron Emission Tomography in dementia of the Alzheimer type. *Arch Intern Med* 1986; 146:2045–2049.
26. Rottenberg DA, Moeller JR, Strother SC, et al. The metabolic pathology of the AIDS dementia complex. *Ann Neurol* 1987; 22:700–706.
27. Phelps ME, Huang SC, Hoffmann EJ, Selin C, Sokoloff L, Kuhl DE. Tomographic measurement of local cerebral glucose metabolic rate in humans with (F-18)-fluoro-2-deoxyglucose: validation of method. *Ann Neurol* 1979; 6:371–388.
28. Reivich M, Alavi A, Wolf A, et al. Use of 2-deoxy D-(1-^{11}C)glucose for the determination of local cerebral glucose metabolism in humans: variation within and between subjects. *J Cereb Blood Flow Metab* 1982; 2:307–319.
29. Phelps ME, Mazziotta JC, Kuhl DE, et al. Tomographic mapping of human cerebral metabolism: visual stimulation and deprivation. *Neurology* 1981; 31:517–529.
30. Reivich M, Gur R, Alavi A. Positron emission tomographic studies sensory stimuli, cognitive processes and anxiety. *Hum Neurobiol* 1983; 2:25–33.
31. Navia BA, Cho ES, Petito CK, Price RW. The AIDS dementia complex: II. neuropathology. *Ann Neurol* 1986; 19:525–535.
32. Donovan Post MJ, Tate LG, Quencer RM, et al. CT, MR and pathology in HIV encephalitis and meningitis. *AJNR* 1988; 9:469–476.
33. Ekholm S, Simon JH. Magnetic resonance imaging and the acquired immunodeficiency syndrome dementia complex. *Acta Radiologica* 1988; 29:227–230.
34. Gurney ME, Heinrich SP, Lee MR, Yin HS. Molecular cloning and expression of neuroleukin, a neurotropic factor for spinal and sensory neurons. *Science* 1986; 234:566–574.