Introduction

The human immunodeficiency virus (HIV) is neurotropic, and most HIV-positive patients develop neurocognitive impairment during the course of their illness, which ranges from HIV-associated minor cognitive motor deficit (MCMD) to HIV-associated dementia (HAD). \(^1,2\)

Reports have shown that patients on highly active antiretroviral therapy (HAART) experience decreases in viral load level\(^3\), reversal of white matter lesions on MR\(^4\), and improvements in neuropsychological test performance\(^5\), but others continue to have progressive neurological impairment despite the HAART regimen and low viral load levels. \(^6\)

Since the central nervous system (CNS) is likely a reservoir site for HIV\(^7\), this may allow for the earliest possible detection of cognitive impairment, and could be used to assess HAART efficacy.

Methods

20 HIV-positive patients (11 men, 9 women, mean age 44.5 yrs) were prospectively studied over a two year period. All of these patients had routine MR imaging including diffusion weighted axial imaging (TR 10000/TE 100/1 NEX) using an echoplanar multislice sequence of 30 interleaved slices of 5mm thickness, matrix 128 X 128, FOV 22cm.

Diffusion was measured in three directions with a b-value of 100,000 s/cm\(^2\) for each direction. Using diffusion-weighted images in three orthogonal directions, an orientation-independent diffusion-weighted image (DWI\(_{trace}\)) is obtained on scanner as follows: DWI\(_{trace} = (DWI_{x}+DWI_{y}+DWI_{z})^{1/3}\).

This trace-weighted image and image without diffusion weighting (S0) are transferred to a workstation. A C program employing the equation (DWI\(_{trace} = S_0\cdot\text{exp}(-bD_{av})\)) is used to calculate the orientation-independent average diffusion maps (D\(_{av}\)) on a pixel-by-pixel basis. \(^8\)

We measured the D\(_{av}\) values of the periventricular white matter, corona radiata, centrum semiovale, genu and splenium of the corpus callosum, and the anterior and posterior limbs of the internal capsule using region-of-interest (ROI) analysis. Typically 20 ROIs (125mm\(^3\)) were placed. Values were compared to normative data (age-matched controls). \(^9\)

We calculated diffusion distribution maps (histograms) from the entire brain using a C-program. The program distributes the pixels to 250 bins with bin widths of 0.02 x 10\(^{-5}\)cm\(^2\)/s. This distribution map was fitted to a three compartment model of: i) brain tissue, ii) cerebrospinal fluid, iii) partial volume using the curve below:

\[
(C_1\cdot\text{exp}(D_{av}\cdot BD_{av}/s^2)) + C_2\cdot\text{exp}(D_{av}\cdot D_{2}/s^2)) + C_3\cdot\text{exp}(D_{av}\cdot D_{3}/s^3)).
\]

Peak location (BD\(_{av}\)) and peak width (s) of the brain tissue compartment were determined from the fitted data. Comparisons of BD\(_{av}\) and D\(_{av}\) for anatomic structures were done using 2-tailed student t-test assuming unequal variance.

Results

All 20 patients had normal brain MR exams except for mild cerebral atrophy. 12 patients had undetectable viral load levels (<400 HIV mRNA copies/mm\(^3\)). 8 patients had elevations in viral load from 10K to 100K HIV mRNA copies/mm\(^3\), and these patients had significantly higher diffusion values compared to the other patients and normals, which are tabulated (Table I). Figure shows comparison of diffusion maps in a patient with undetectable viral load versus a patient with elevated viral load.

Discussion

In HIV-positive patients, diffusion histograms and diffusion constant (D\(_{av}\)) calculations can detect abnormalities within the periventricular white matter, corpus callosum, internal capsule, and centrum semiovale bilaterally. Thus, MRDTI and diffusion distribution analysis may have a role as a marker of HIV disease progression and HAART efficacy.

Acknowledgments

This work was supported in part by a grant from the Radiological Society of North America.

References


Table I: Diffusion Measurements (10\(^{-5}\) cm\(^2\)/s)

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Patients with Undetectable Viral Load (n=12)</th>
<th>Patients with Elevated Viral Loads (n=8)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PVWM right</td>
<td>0.820</td>
<td>0.877</td>
<td>P&lt;.050</td>
</tr>
<tr>
<td>PVWM left</td>
<td>0.832</td>
<td>0.914</td>
<td>P=.015</td>
</tr>
<tr>
<td>genu CC</td>
<td>0.809</td>
<td>0.927</td>
<td>P=.042</td>
</tr>
<tr>
<td>PLIC right</td>
<td>0.755</td>
<td>0.804</td>
<td>P=.035</td>
</tr>
<tr>
<td>PLIC left</td>
<td>0.744</td>
<td>0.817</td>
<td>P=.003</td>
</tr>
<tr>
<td>Centrum</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Semiovale left</td>
<td>0.749</td>
<td>0.804</td>
<td>P=.015</td>
</tr>
<tr>
<td>Centrum</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Semiovale right</td>
<td>0.746</td>
<td>0.800</td>
<td>P=.026</td>
</tr>
<tr>
<td>BD_{av}</td>
<td>0.742</td>
<td>0.782</td>
<td>P&lt;.001</td>
</tr>
</tbody>
</table>