Quantitative MRI Study of Non-cognitively Impaired HIV Patients Shows No Detectable Neurodegeneration

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Aims: To establish whether diffusion tensor imaging (DTI), magnetization transfer ratio (MTR) or spectroscopy (MRS) can identify subtle neurodegeneration in non-cognitively impaired HIV patients (treated and untreated), compared to healthy (HIV negative) volunteers.

Background: It is known that HIV infects the central nervous system (CNS) early after infection. If untreated, CNS infection results in significant cognitive deficit (e.g. AIDS dementia complex). Although HIV treatment (such as HAART) controls peripheral viral replication there is some doubt whether the drug is able to penetrate the CNS. The quantitative MRI techniques DTI, MTR and MRS have shown they offer the possibility of identifying subtle changes in normal-appearing brain in neurodegenerative diseases such as MS [1]. We used these techniques to determine whether non-cognitively impaired HIV patients (both treated and untreated) exhibit detectable brain damage compared to healthy volunteers. Regular QA shows that the scanner delivers excellent repeatability with a normal variation in MTR being one of the best of published MTR studies [2].

Methods: We recruited 36 participants (all males, age 30-50 years) in three groups: Group A (untreated HIV+, CD4=300-500; N=12), Group B (treated HIV+, CD4 < 40; N=12), Group C (healthy (HIV–) gay men; N=12). Subjects underwent a cognitive test to show they are not cognitively impaired. Scanning was conducted on a Siemens Avanto 1.5 T MR imager. Three quantitative imaging techniques were employed: MTR (3D gradient echo, TR=30 ms, TE=5 ms, FA=5, FOV=220 x 220 mm^2, matrix=256x192, partition thickness=2.5 mm, MT pulse FA=500°, scan time=2x6 mins), DTI (EPI, TR=6400 ms, TE=111 ms, FOV=220 x 220 mm^2, matrix=128x128, slices=34, thickness=4 mm, 30 diffusion directions, b=1000s/mm^2, averages=2, scan time=6.5 mins), MRS (svs in frontal white matter, TR=1500 ms, TE=135 ms, averages=192, FID=1024 points, voxel size=20x20x20 mm^3, BW=1 kHz, scan time=5 mins). A high-resolution T1-weighted MP-RAGE dataset was used to segment the brain into white matter, grey matter and whole brain (white+grey) compartments. Apparent diffusion coefficient (ADC), fractional anisotropy (FA) and MTR histograms were constructed and histogram peak height, position and means were analyzed to identify potential group differences [3]. MRS data was used to measure relative concentrations of choline (Cho), creatine (Cr) and N-acetylaspartate (NAA) using the jMRUI software package [4]. Grey/white matter proportions in the MRS voxel were used as covariate in the final statistical analysis of group differences.

Table 1
Group differences in mean MTR, ADC and FA of white matter (WM), grey matter (GM) and whole brain (WB). In spite of good reproducibility (shown by our low sd), group differences are too small compared to the standard error from our control group indicating that there are no detectable differences in the brain at this stage of the disease (all data given to 3 sig. fig.).

Group Difference	Diff in mean MTR (pu)			Diff in mean ADC (10^{-12} m^2s^{-1})			Diff in mean FA		
	WM	GM	WB	WM	GM	WB	WM	GM	WB
Untreated-controls	-0.0799	-0.104	-0.0687	-1.96	0.829	3.41	-0.00186	0.00398	-0.00534
Treated-controls	0.0704	0.145	0.0928	5.03	1.01	3.92	-0.00456	0.00447	-0.00315
SE of control mean	0.178	0.163	0.112	6.31	6.59	6.651	0.00440	0.00155	0.00306

Results and Discussion: Our study shows that non-cognitively impaired HIV+ patients do not exhibit significant differences in measures of MTR, ADC and FA (Table 1) irrespective of whether they have undergone treatment. Our data show that the normal standard deviation (sd) in mean WM MTR for this study is 0.50 pu, demonstrating good reproducibility that compares favourably with other published MTR studies, which report sd ranges from 0.4 to 1.0 pu [2]. Group differences for mean MTR, ADC and FA are shown in Table 1 together with the standard error (SE) for the histogram mean of our control group. The observed group differences are too small compared to the SE, indicating that it is not possible to distinguish group differences, despite the good reproducibility of our MTR and DTI measurements. In addition, no statistically-significant group differences were found for histogram peak height or peak position. MRS shows there may be a trend toward higher Cho:Cr ratio and lower NAA:Cr for the HIV groups (which signifies subtle white matter damage), but these differences are not large enough to be statistically significant. The Cho:NAA ratio is also non-significant with these modest group sizes.

Conclusions: Both treated and untreated non-cognitively-impaired HIV patients do not suffer detectable brain damage using reliable MTR, DTI and MRS measurement techniques at 1.5 T.

References
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