Micro-structural alterations in the brain of well-treated HIV+ patients with minor neurocognitive disorders: a multi-contrast MRI study at 3T.

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**Background:** Since the introduction of highly active antiretroviral therapies (HAART), the prognosis of HIV patients has improved but the prevalence of minor neurocognitive disorders (MND) has increased1. The physiopathology of MND is, however, not clear as well as the reasons why some well treated patients suffer from MND and others not. In this study, we used a multi-contrast MRI based approach at high field, in order to test the hypothesis that well-treated aviremic MND+ HIV+ patients present different brain microstructural characteristics compared to MND- HIV+ patients and healthy controls (HC).

**Methods:** We enrolled 17 MND+ and 19 MND- patients with undetectable HIV-1 RNA and 14 age-matched HC. MRI was performed in a 3T Trio machine (Siemens, Erlangen, Germany) equipped with a 32 channel coil. The protocol included: high-resolution MPRAGE (TR/TE = 2400/3 ms, voxel size = 1x1x1.2 mm3, FoV = 256x240x160), MP2RAGE (TR/TE = 5000/3 ms, inversion time = 700 ms, FA = 4°, voxel size = 1x1x1.2 mm3, FoV = 256x240x160) and Magnetization transfer (MT, TR/TE = 48/23 ms, voxel size = 2x2x2 mm3, FoV = 240x256x96, 8 echoes). In addition, we acquired Susceptibility Weighted Images (SWI) using a velocity compensated 3D gradient echo sequence (TR=50/30 ms, FA = 18°, voxel size 0.7x0.7x1.4 mm3, FoV = 180x220x52) and a high pass filter to obtain images without low-frequency phase variations. T1 maps were derived from the MP2RAGE and MT ratio was computed as follows: MTR = (M0-MT)/M0*100; T2* maps were obtained from the multi-echo MT acquisition. All quantitative maps were linearly registered to the MPRAGE volume using ELASTIX.2 Regions of interest (ROIs) were automatically extracted for white and gray matter (WM, GM), thalamus, basal ganglia (caudate, putamen and globus pallidus) and hippocampus using an in-house software based on variational expectation-maximization tissue classification3-4. Concerning SWI images, ROIs were manually positioned in the three basal ganglia and the thalamus. Statistical analysis used univariate and multivariate permutation-based Hotelling tests and correction for family-wise error rate. A linear discriminant analysis between MND+ and MND- patients was performed using multi-parametric MRI data and cross-validated with a leave-one-out test.

**Results:** Univariate analysis revealed that MND+ patients had lower MTR than MND– and HC reaching significance in WM (p=0.02) and caudate (p=0.01), fig 1 and 2. Multivariate analysis based on T1, MTR and T2* showed significant differences between MND+ and MND- patients in WM and GM (p=0.02 respectively) and between MND+ and HC in the caudate (p=0.02). SWI data were not included in the multivariate analysis, since they were not available for all the HC (n=8). The linear discriminant analysis based on T1, MT and SWI data distinguished MND + and MND-patients with a classification quality of 0.73% after cross-validation.

**Conclusion:** Our findings show the presence of micro-structural brain alterations in well treated HIV+ MND+ patients compared to MND- and HC, suggesting loss of structural integrity. In addition, they suggest that a multi-contrast MRI approach at high field may be a powerful approach to understand the physiopathology of MND and to discriminate between patients’ sub-groups.


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![Fig 1: T1, MTR and T2* mean values in WM, GM, thalamus and hippocampus. * p<0.05](image1)

![Fig 2: T1, MTR and T2* mean values in the basal ganglia. ** p≤ 0.01](image2)