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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 increased[1]. 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 mm^3, FoV = 256x240x160), MP2RAGE (TR/TE = 5000/3 ms, inversion time = 700 ms, FA = 4°, voxel size = 1x1x1.2 mm^3, FoV = 256x240x160) and Magnetization transfer (MT, TR/TE = 48/23 ms, voxel size = 2x2x2 mm^3, 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 mm^3, 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 classification[3-4]. 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.

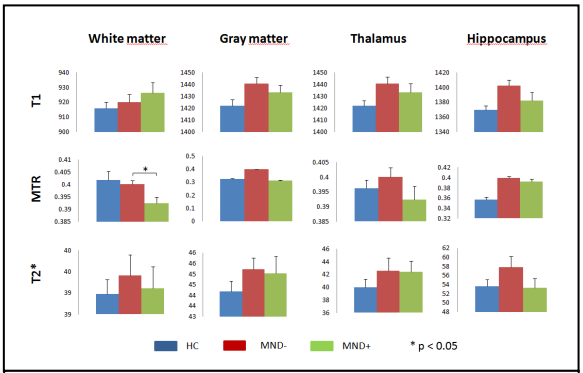

Fig 1: T1, MTR and T2* mean values in WM, GM, thalamus and hippocampus. * p< 0.05

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.

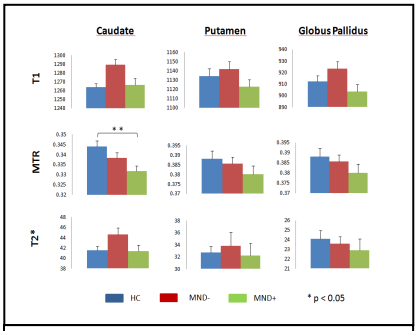

Fig 2: T1, MTR and T2* mean values in the basal ganglia. ** p≤ 0.01

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.

References: 1. Antinori A., et al., Neurology 2007 ; 2. Klein et al, IEEE Transactions on Medical Imaging 2010 ; 3. Ribes et al., ISMRM 2011 ; 4. Roche et al., Medical Image Analysis 2011.

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