Mapping Gray Matter Structural Integrity in Adults Perinatally infected with HIV

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Target Audience: Researchers using imaging and neurocognitive methods to evaluate the impact of HIV on the brain.

Purpose: To evaluate the long term impact of persistent reservoirs of HIV in the CNS and the potential effects of long term use of some of its antiretroviral therapeutics on the tissue structural integrity of the brain subcortical- and deep-gray matter (GM) regions in people living with HIV infection. In this study, a whole-brain diffusion kurtosis imaging (DKI) method is used to obtain mean diffusivity (MD) and mean kurtosis (MK) metric maps in adults perinatally infected with HIV and a matched community control group for comparisons.

Methods: MRI data were acquired from 24 adults perinatally infected with HIV (mean±SD: 20±1.9 years) and 9 control subjects (mean±SD: 22±1.4 years) using a 3 Tesla scanner. The MR protocol included DWI (b: 0, 1000, 2000 s/mm^2; no. of diffusion gradient directions: 30; TR: 6100 ms; TE: 101 ms; slices: 45; resolution: 2.7 mm isotropic; 2 ave) and T2 (for distortion correction) sequences. Data were processed using DKE[1] and DtiStudio (www.mristudio.org). The DKE-processed maps of MD and MK were spatially transformed to a template in MNI space at 1 mm resolution. To obtain data from GM regions in these maps, we used a brain atlas[2] with 130 regions-of-interest (ROI). Furthermore, to avoid inclusion of voxels with predominantly CSF or white matter (WM) in the ROIs, a GM mask was created for each subject by setting appropriate thresholds in their MD and FA images, respectively. Finally, data were selected only from 60 predominantly GM ROIs for analysis. Between group analysis of MD and MK metrics of the ROIs was carried out using ANCOVA with age and sex as covariates. A p value of <0.05 was considered significant.

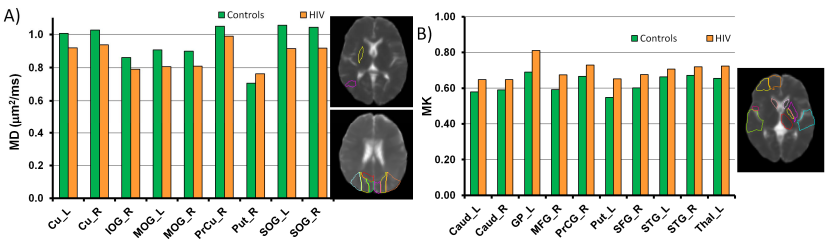

Figure 1: Brain GM ROIs with significant MD (A) and MK (A) changes in the HIV group compared to controls. The images show the ROIs.

Results: In Figure 1A are shown the mean MD values of nine GM ROIs that showed significant changes in the HIV group. The nine ROIs comprised of cuneus - left (Cu_L) and right (Cu_R), inferior occipital gyrus right (IOG_R), middle occipital gyrus - left (MOG_L) and right (MOG_R), pre-cuneus right (PrCu_R), putamen right (Put_R), and superior occipital gyrus - left (SOG_L) and right (SOG_R). In Figure 1B are shown ten GM ROIs with significant mean MK changes in the HIV group. The ten ROIs included caudate nucleus - left (Caud_L) and right (Caud_R), globus pallidus left (GP_L), middle frontal gyrus right (MFG_L), precentral gyrus right (PrCG_R), putamen left (Put_L), superior frontal gyrus right (SFG_R), superior temporal gyrus - left (STG_L) and right (STG_R), and thalamus left (Thal_L). In the HIV group compared to controls, the MD values were lower across the ROIs, except in Put_R, and the MK values were consistently higher in all the ROIs.

Discussion: The significant changes observed in the MD and MK metrics of the subcortical and deep GM brain regions in people with HIV infection indicate that these regions are also affected in addition to previously known WM regions. Furthermore, there was no overlap of the ROIs found with significant MD and MK changes; it indicates that the tissue water in these ROIs experiences different degrees of Gaussian and non-Gaussian diffusion effects. The significantly reduced MD values and increased MK values in the GM ROIs indicate that tissue structural and cellular compositional changes occur in the intra- and extra-cellular environments of the brain of individuals with HIV infection.

Conclusion: Microstructural changes occur in the subcortical and deep GM brain regions of adults infected with HIV. These changes indicate underlying cellular pathologies that may be responsible for HIV-associated neurocognitive disorder (HAND) prevalent in people living with HIV infection. The neuroimaging methodology described here will be useful in developing biomarkers for evaluating the impact of HIV and its therapeutics.

References: 1). Tabesh A, Jensen JH, Ardekani BA, Helpern JA. *Magn Reson Med* 2011; 65:823-836. 2) Oishi K, Faria A, Jiang et al. *NeuroImage* 46:486-499 (2009).

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