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Whole-brain structural network reorganization in HIV

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ABSTRACT

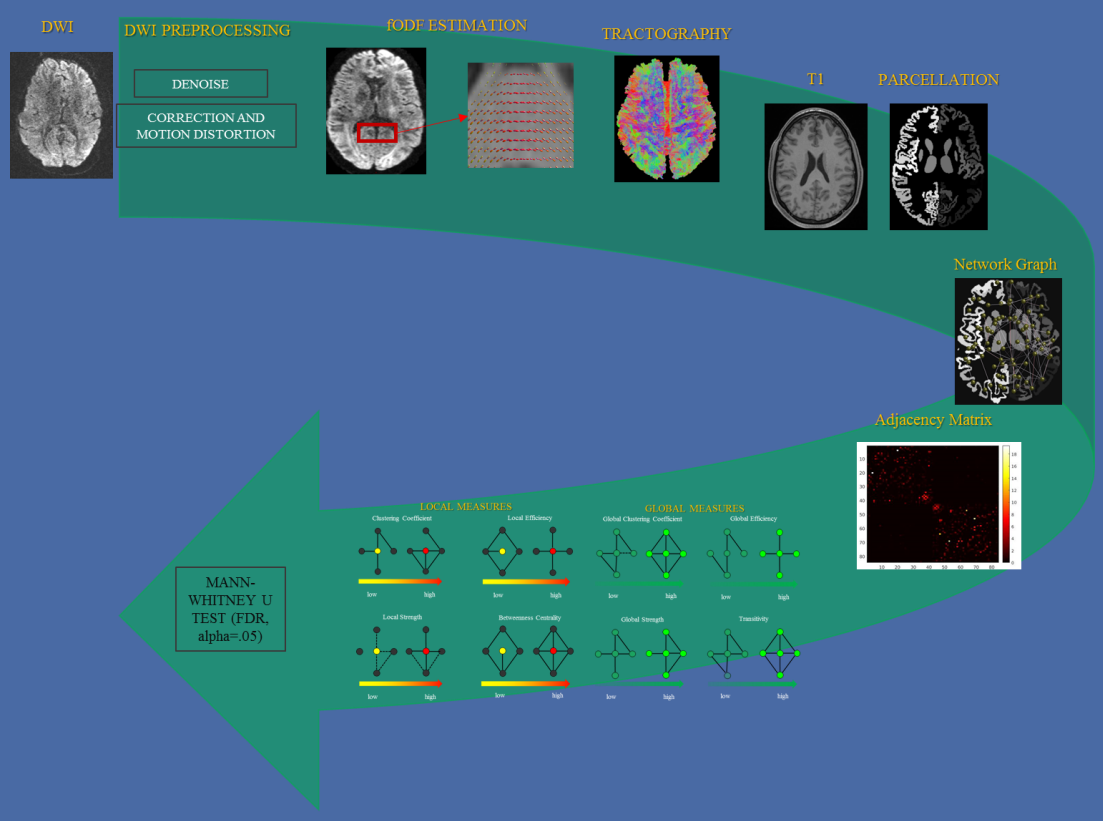
The human immunodeficiency virus (HIV) causes an infectious disease with a high viral tropism toward CD4 T-lymphocytes and macrophage. Since the advent of combined antiretroviral therapy (CART), the number of opportunistic infectious disease has diminished, turning HIV into a chronic condition. Nevertheless, HIV-infected patients suffer from several life-long symptoms, including the HIV-associated neurocognitive disorder (HAND), whose biological substrates remain unclear. HAND includes a range of cognitive impairments which have a huge impact on daily patient life. The aim of this study was to examine putative structural brain network changes in HIV-infected patient to test whether diffusion-imaging-related biomarkers could be used to discover and characterize subtle neurological alterations in HIV infection. To this end, we employed multi-shell, multi-tissue constrained spherical deconvolution in conjunction with probabilistic tractography and graph-theoretical analyses. We found several statistically significant effects in both local (right postcentral gyrus, right precuneus right inferior parietal lobule, right transverse temporal gyrus, right inferior temporal gyrus, right putamen and right pallidum) and global graph-theoretical measures (global clustering coefficient, global efficiency and transitivity). Our study highlights a global and local reorganization of the structural connectome which support the possible application of graph theory to detect subtle alteration of brain regions in HIV patients.

INTRODUCTION

The human immunodeficiency virus (HIV) is an infectious disease with a high viral tropism toward CD4 T-lymphocytes and macrophage. The new combined antiretroviral therapy (CART) has greatly reduced the incidence of opportunistic infections, transforming the HIV into a chronic condition. The incidence of HIV-associated neurocognitive disorder (HAND) is still an important problem in the everyday life of HIV patients [1]. Structural connectivity is described as the presence of physical connection among brain regions constituted by white matter tracts. It is commonly estimated using diffusion weighted imaging (DWI), which allows the indirect reconstruction of the brain white matter (WM) fibers based on estimating the probabilistic displacement profile of water molecules in tissue. Using spherical deconvolution [2], and in particular the recently introduced multi-shell, multi-tissue constrained spherical deconvolution [3] technique allows a more accurate estimation of the fiber orientation distribution function (fODF) through the usage of intrinsically generated maps for WM, gray matter (GM) and cerebrospinal fluid (CSF). Also, brain network are often represented as graphs and subsequently analysed using graph-theoretical tools [4]. It has been shown that metrics which summarize e.g. graph topology, efficiency, clustering etc. can convey important information about brain network reorganization.
The aim of this study was to examine putative structural brain network changes in HIV-infected patient to test whether diffusion-imaging-related biomarkers could be used to discover and characterize subtle neurological alterations in HIV infection.

METHODS

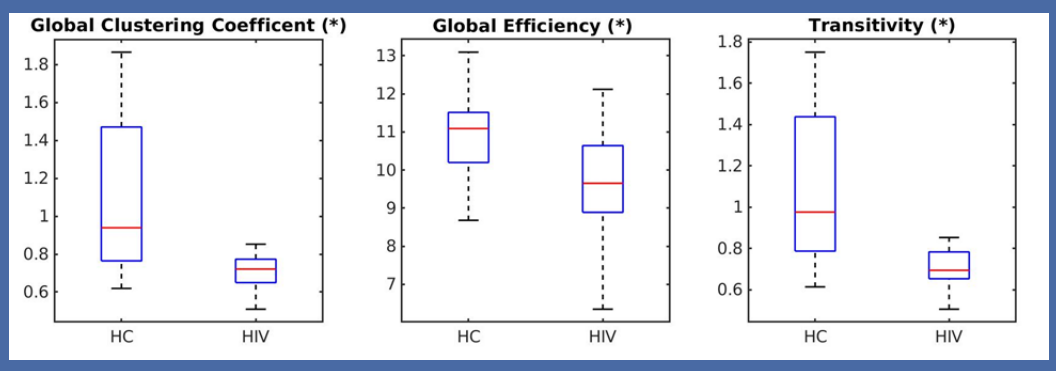
We enrolled 15 HIV infected patients and 15 age matched healthy controls (HC). For each participants we acquired a MPRAGE and a multi-shell diffusion weighted image (b-value 1000 and 2500) (SP-EPI single shot). For each subjects, after pre-processing of the data, we estimated the fODF and created a tractograms. We then built an adjacency matrix using the latter in conjunction with a parcellated image. Finally we calculated local and global metrics and compared these metrics between the two groups (HIV vs HC) using the Mann Whitney U Test



RESULTS

We found statistically significant differences between the HIV-infected group and the control group in both local and global metrics.

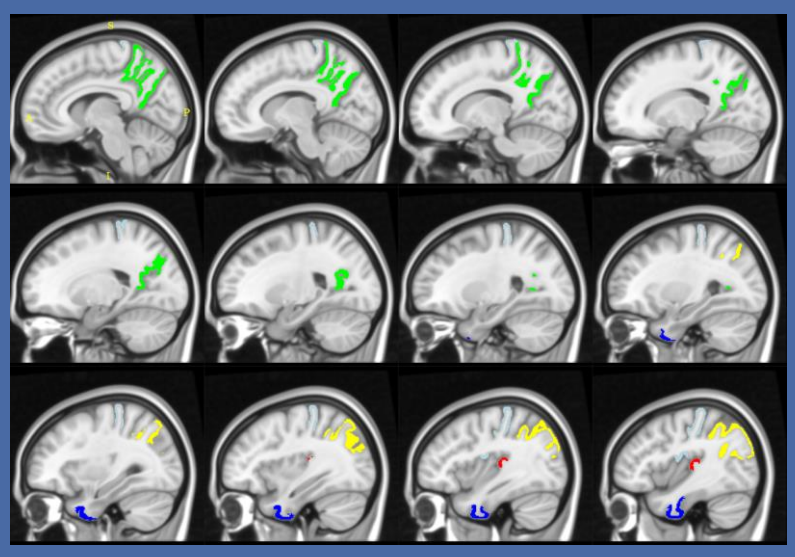
Global Metrics



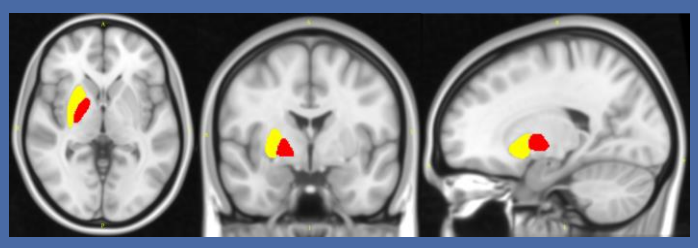
Global metrics in which group-wise, statistically significant differences were found. HC= healthy controls. (*) p<0.05

Local Metrics

We found statistically significant differences in betweenness centrality in the right inferior temporal gyrus (p=.015, HIV>HC), in the right transverse temporal gyrus (Herschel gyrus) (p=.005, HC>HIV) and in the right pallidum (p=.04, HC>HIV). Differences were also observed in local strength. Additionally, we found statistically significant differences in both local clustering coefficient and local efficiency in the right pallidum (clustering coefficient p= .01 HC>HIV, local efficiency p= .007 HIV>HC), in the right putamen (clustering coefficient p= .005 HC>HIV, local efficiency p= .007 HIV>HC), in the right inferior parietal lobule (clustering coefficient p= .004 HC>HIV, local efficiency p= .007 HIV>HC), in the postcentral gyrus (clustering coefficient p= .004 HC>HIV, local efficiency p= .003 HC>HIV) and in the precuneus (clustering coefficient p= .007 HC>HIV, local efficiency p= .01 HIV>HC)



Brain regions that present statistically significant differences in local metrics (S=superior, I=inferior, A=anterior and P=posterior). Legend: precuneus (green), transverse temporal gyrus (red), inferior parietal lobule (yellow), inferior temporal gyrus (blue) and post-central gyrus (light blue). See table II for effect sizes and directions.



Brain regions that present statistically significant differences in local metrics (L=left, R=right, A=anterior and P=posterior). Legend: Putamen (yellow) and Globus Pallidus (red).).

CONCLUSION

Our study highlights a global and local reorganization of the structural connectome in HIV patients compared to HC, with involvement in several regions that subserve functions which are known to be impaired in HAND. Our findings therefore point toward the possibility of examining and monitoring disease presence and progression, and in particular brain involvement, in HIV-infected patients.

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