Brain network reorganization in HIV infection

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Background

HIV

❑ Approximately 38 million people were living with **human immunodeficiency virus**, with 1.7 millions of newly infected patients.

cART

❑ While the introduction of **combined antiretroviral therapy** decreased the number of deaths related to HIV complications, new infection rate has been steadily increasing.

❑ cART determined a change in the course of HIV infection, transforming it into a chronic condition

HAND

❑ At least 50% of HIV-infected patients are susceptible to developing cognitive, motor and behavioural disorder, globally known as **HIV-associated neurocognitive disorders**, which determines significant impairment of the life quality even when viremia is under control.

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Aim

Objective neuroimaging-based biomarkers are highly desirable to detect, quantify and to monitoring HAND

Resting-state functional MRI is a powerful tool to measure the brain functional activities in different neurological networks

To study a putative functional reorganization in HIV positive patients through graph theory and the disruption index
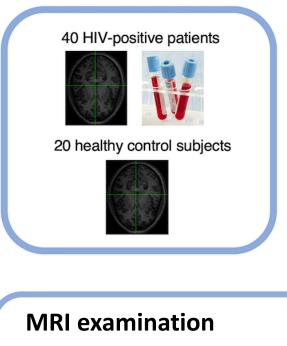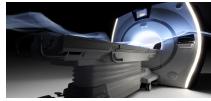
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M&M: subjects

40 HIV-positive patients

20 healthy control subjects

MRI examination

3T scanner system
rs-fMRI
MPRAGE
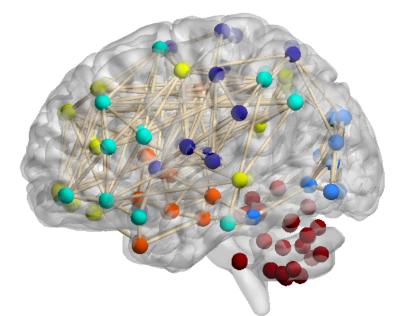
	HIV positive patients	healthy control subjects
Subject number	40	20
Age in years		
Average [range]	40.4 [26-65]	44.1 [27-64]
Sex (male/female)	32/8	11/9
Ethnicity, n (%)		
Caucasian	36 (90%)	20 (100%)
Hispanic	2 (5%)	-
African	2 (5%)	-
Risk factors, n(%)		
Heterosexual	19 (47.5%)	20 (100%)
Homosexual	20 (50%)	-

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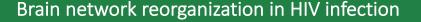POLICLINICO TOR VERGATA

M&M: Graph theory

Graph theory is used to study both local and global properties of the complex brain networks.

The brain network is conceptualized as a **graph**, in which brain regions represent *nodes* and the relationships between the regions represent *edges*.

Global and Local network property

Degree
Betweenness Centrality
Global efficiency
Local efficiency
Clustering coefficient
Transitivity
Modularity

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To evaluate the alterations of *local measure* is used the **disruption index k**

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To evaluate the alterations of *local measure* is used the **disruption index k**

for example **Degree**

x axis →The mean degree of each node in the control group

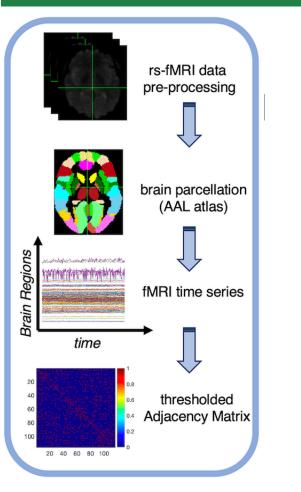y axis → the difference between groups in mean degree of each node

<HIV group> - <Control group>

< Control group>

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SOCIETÀ ITALIANA DI FISICA
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To evaluate the alterations of *local measure* is used the **disruption index *k***

for example **Degree**

x axis →The mean degree of each node in the control group

y axis → the difference between groups in mean degree of each node

<HIV group> - < Control group >

< Control group>
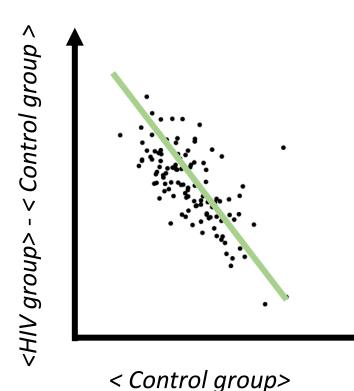
The slope of the linear regression to the data is the **disruption index *k***

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M&M: Data Analysis

❑ Motion correction, distortion correction, slice timing correction, nonlinear coregistration between preprocessed functional scans and standard space through the T1 weighted MPRAGE image.

❑ The whole brain has been parceled out in 116 regions through automated anatomical labeling (AAL) atlas.

❑ Average of the rs-fMRI signal in each region were extracted.
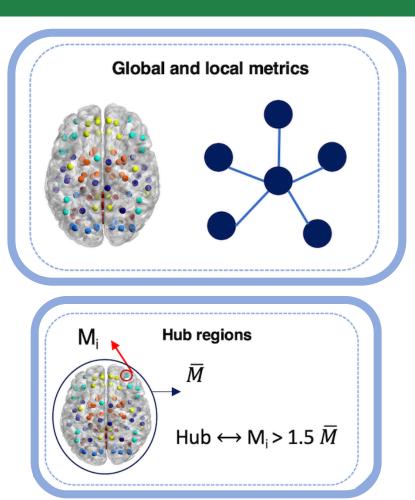❑ Partial correlation between all 116 timeseries was used to generate subject-wise adjacency matrices.

❑ Adjacency matrices were thresholded at 10% density
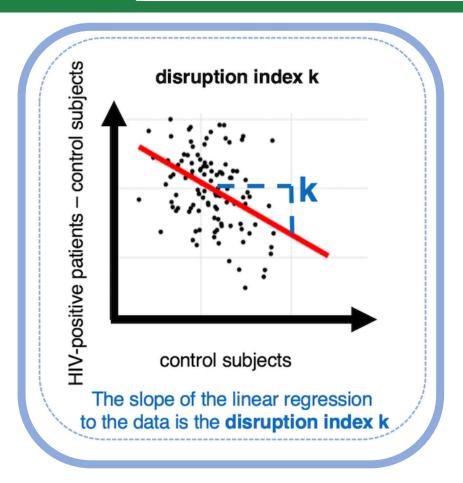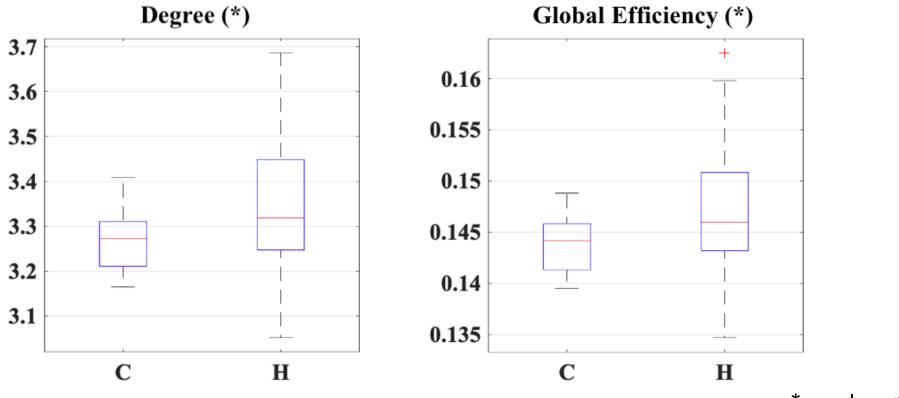
Results: Global metrics

* p-value <0.05

Results: Disruption index k
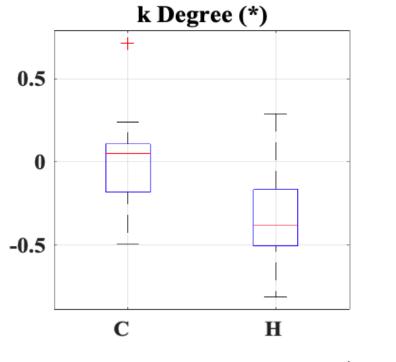
k Betweenness Centrality (*)

* p-value <0.05

Results: Disruption index k

* p-value <0.05

Results: Disruption index k

k Clustering Coefficient (*)

* p-value <0.05

Results: Disruption index k
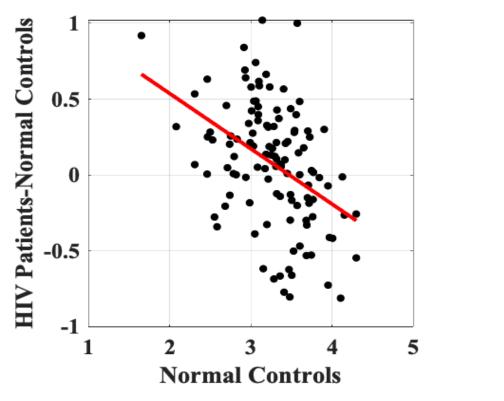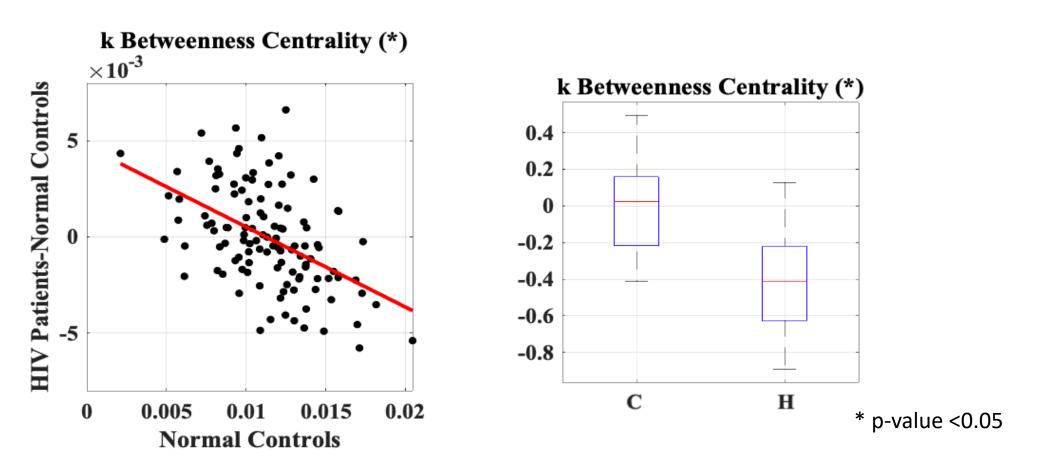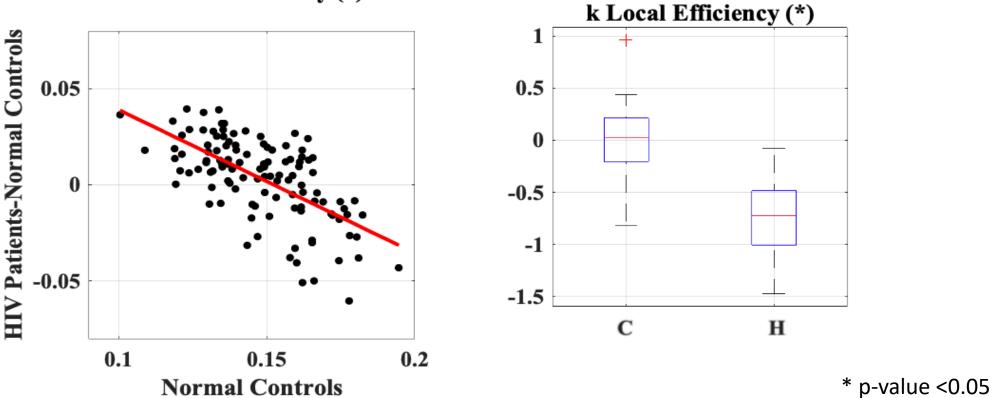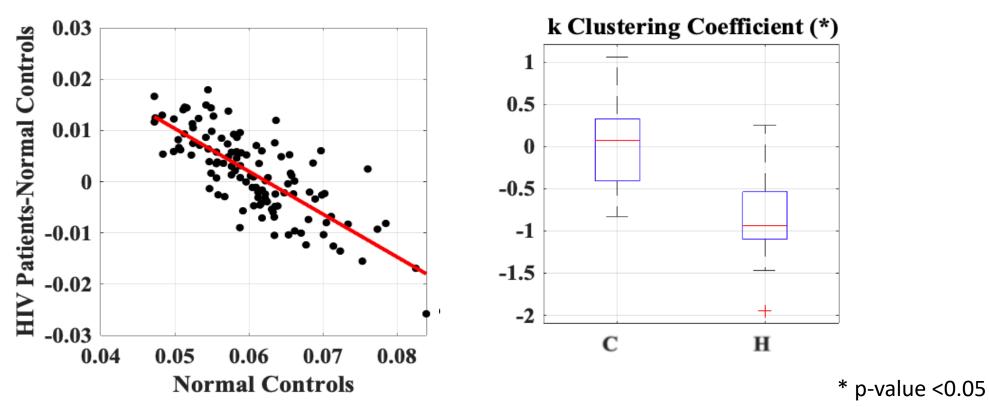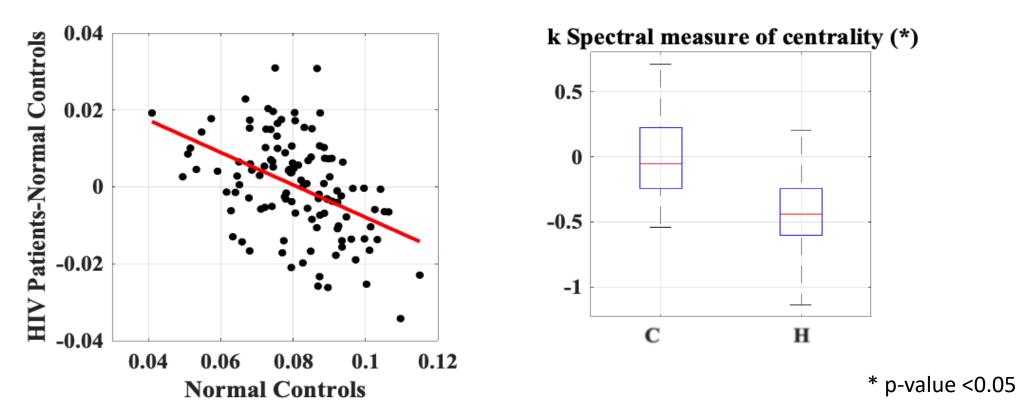
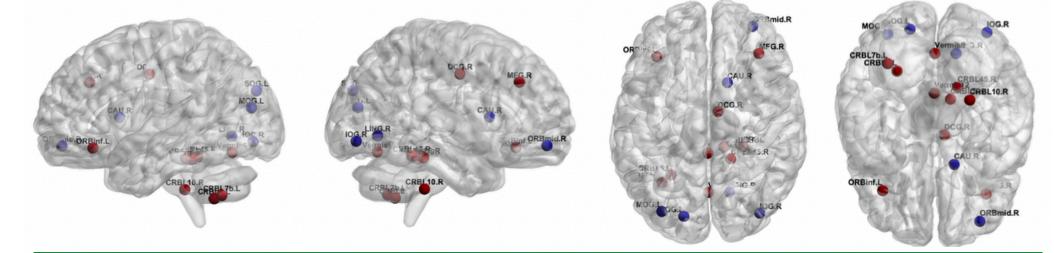k Spectral measure of centrality (*)

* p-value <0.05

Results: HUB

Ten hub regions **disappear** in HIV patients as compared to controls:

Cerebellum

× Right lobule III of cerebellar hemisphere;

× Right lobule IV, V of cerebellar hemisphere;

× Left lobule VIIB of cerebellar hemisphere;

× Left lobule VIII of cerebellar hemisphere,

× Right lobule X of cerebellar hemisphere.

Frontal lobe

× Right Middle frontal gyrus;

× Left Inferior frontal gyrus, orbital part;
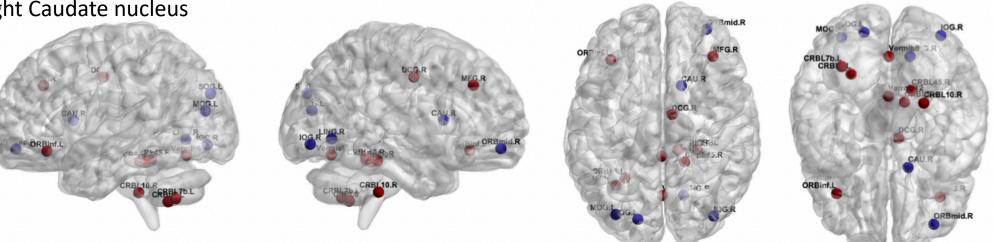
× Right Median cingulate and paracingulate gyri;

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Six hub regions **appear** in HIV patients as compared to controls:

✓ Right Middle frontal gyrus, orbital part → **frontal lobe**

✓ Right Lingual gyrus → **occipital lobe**

✓ Left Superior occipital gyrus → **occipital lobe**

✓ Left Middle occipital gyrus → **occipital lobe**

✓ Right Inferior occipital gyrus → **occipital lobe**

✓ Right Caudate nucleus

Conclusions

❑ The differences in local network measures highlight cerebral reorganization of brain networks in HIV patients.

❑ Interestingly, the regions in which we found reorganized hubs are integrated into neuronal networks involved in working memory, motor and executive functions often altered in patients with HAND.

❑ Moreover, the involvement of cerebellum highlight the deep involvement of the CNS in HIV patients.