Disrupted Cortical Connectivity in the Aging HIV+ Population

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Background

Brain decline is of increasing concern in the HIV+ population; over half of those living with HIV (in the US) will be over age 50 by 2015. Combination anti-retroviral therapy (cART) has extended the lives of many sufferers of this viral epidemic. The effect of HIV on brain connectivity is poorly understood. Here we used high angular resolution diffusion imaging (HARDI) to map whole-brain structural connectivity in elderly HIV patients and controls.

As the ApoE4 genotype is a well-known risk factor for Alzheimer’s disease (AD) – tripling the risk compared to non-carriers - we also examined whether carrying ApoE4 modulated the effect of HIV on cortical networks.

The human brain is a complex network of structural and functional interconnections, with diverse regions activated during functional tasks. Advanced diffusion imaging methods, which track the diffusion of water along the brain’s axons, can reveal dense microstructural fiber bundles connecting anatomically distinct cortical and subcortical regions.

Results

HIV+ patients show different patterns of connectivity.
- Superior frontal cortices
- Non-significant tested connections are in black.
- Significantly different inter-cortical connections (blue lines):
  - R superior frontal and R precentral cortex,
  - R precentral cortex and R posterior cingulate,
  - R posterior cingulate and L superior frontal cortex
  - R inferior parietal and R isthmus of the cingulate
- The strength of connections (total fiber density of connections for each region) is significantly lower in HIV+:
  - L paracentral
  - L & R posterior cingulate
  - L & R superior frontal
  - R caudal anterior cingulate.

HIV+ carriers of the ApoE4 allele (N=9) vs HIV+ non-carriers (N=46)
- Lower mean FA:
  - right inferior and medial temporal gyri
  - left and right precuneus

- Local efficiency
  - left precenral- gyrus
  - left precuneus
  - R superior parietal cortex

Methods

Imaging: MRI and 64-directional HARDI were collected at 3 Tesla from 55 HIV-infected participants compared to 30 age and sex-matched controls (age: 60-80; 82M/3F). 9 of 55 patients (16.4%) were ApoE4 carriers.

Cortical Surface Extraction: 35 regions per hemisphere (70 per brain) extracted using FreeSurfer software. Surfaces dilated for optimal coverage.

Image Processing: DWIs were corrected for eddy current distortions. DWI images were aligned to their corresponding T1 images using elastic registration [Leow et al. 2007]. Deformations were applied to fibers [Jahanshad et al., 2011]. Hough transform based tractography was performed using ODFs by probabilistically seeding voxels [Aganj et al, 2011].

Connectivity and network measures: Network analysis of normalized counts of fibers passing through and between each cortical region were used to create connectivity matrices. The mean FA was also calculated for all connecting tracts and mean FA matrices were created. We calculated strength, or the weighted number of connections, and efficiency of each node, using the Brain Connectivity Toolbox [Rubinov and Sporns 2010].

Statistics: If more than 50% of subjects had no detectable fibers connecting the regions, then the connection was not linear regression was performed to assess effects of HIV diagnostic status and the dominant effect of the ApoE4 genotype (adjusting for effects of age and sex). For multiple comparisons corrections over the number of matrix elements tested for differences, we used FDR at q<0.05.

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