Imaging Methods for NeuroAIDS

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Neuroimaging as a Biomarker

- Provide another window into the neurological effects of HIV, non-invasively identifying biomarkers of injury
  - Better define the neuropathogenesis of HIV
  - Monitor disease progression
  - Enable more accurate diagnosis and identification of at-risk individuals
  - Guide treatment and monitor therapeutic intervention

- Magnetic Resonance Imaging (MRI) allows the study of HIV-related effects on brain structure, metabolite concentration, and white matter integrity
What neuroimaging may tell us about the impact of HIV on the CNS

- What are the common characteristics of neuropathogenesis in the current era?
- Is history of severe immunosuppression (CD4 nadir) associated with tissue damage or loss?
- How does the brain respond during immune recovery, and does this impact cognition or functional performance?
- Does the combination of HIV and a psychiatric disorder increase the likelihood of brain injury?
- Can patterns of abnormalities classify individuals at greatest risk for cognitive decline?
Progressive White Matter Damage in HIV

- Simple description of change over one year

Fennema-Notestine, preliminary CHARTER
Lower Nadir CD4 and Structural Damage

- Must consider multivariable models

Jernigan et al. 2011
Factors Associated with Brain Alterations

- Metabolic Status
- Psychiatric Diagnosis
- Cognition
- Genetics
- Age
- CSF Biomarkers
- Treatment Effects
- Immune Status

Neuroimaging Measures
Common MRI Modalities

- Anatomical / Structural MRI
  - Size of neuroanatomical structures and volume of CSF spaces provide indices of tissue damage, loss, and inflammation

- MR Spectroscopy
  - Samples metabolite levels to assess neuronal integrity and inflammation

- Diffusion Tensor Imaging
  - Integrity of white matter fibers
Anatomical

T1  T2  PD
Structural Volumes

Abnormal White Matter
Total White Matter
Ventricular CSF

Cortical Gray
Subcortical Gray
Sulcal CSF
Basal Ganglia and White Matter Damage in HIV

- **White matter pathology**
  - Volume loss, even on treatment, associated with detectable HIV CSF RNA viral load and lower nadir CD4
  - Increased abnormalities are associated with lower nadir CD4 and postmortem markers of dendritic loss

- **Basal Ganglia damage**
  - Caudate atrophy and subcortical volume loss associated with lower nadir CD4 and neurocognitive impairment

- **Abnormalities linked to increasing CD4 during recovery while on effective ART**

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Fennema-Notestine et al. 2011
MR Spectroscopy Metabolites

- **N-acetylaspartate (NAA):** neuronal integrity
- **Choline/choline-containing compounds (Cho):** cell membrane degradation and lipid changes
- **Myo-inositol (MI):** glial proliferation / inflammation
- **Creatine/phosphocreatine (Cr):** energy stores
Common regions of interest in HIV

- Frontal White Matter
- Frontal Gray Matter
- Basal Ganglia
Decreased Neuronal Integrity and Increased Inflammation in HIV

- **Neuronal injury** evident in sampled regions of basal ganglia and frontal lobe (reduced NAA)
  - May be associated with decreasing current CD4

- **Inflammation** suggested by higher levels of CHO and MI
  - May be predicted by inadequate viral suppression in CSF at baseline

Fennema-Notestine, Taylor et al., preliminary CHARTER
Diffusion Tensor Imaging (DTI)

- Quantifying motion of water molecules
- Fractional anisotropy (FA), a scalar value of the degree of anisotropy (directional variation)
White Matter Fiber Tracts

- Alterations in white matter integrity modify typical diffusion properties
Abnormal White Matter Integrity in HIV

- Reports of altered FA support white matter damage, when studying the large bundles in corpus callosum and frontal regions, even on ART.
- Altered FA is associated with neurocognitive impairment, current CD4, and HIV viral load.
- Caudate and putamen also demonstrate abnormal diffusion properties.
Explorations in HIV

- White matter and basal ganglia injury remain common, including evidence for neuronal loss and inflammation.

- Lower CD4 nadir associated with tissue loss, reduced neuronal integrity, and white matter damage.

- Suggestions of inflammation in white matter and subcortical gray are being explored in association with cognition.

- Studying whether history of severe trauma influences presentation of HIV in the brain (S. Seedat, South Africa).

- Broad interest in predicting cognitive decline to ensure timely treatment.
Magnetic Resonance Imaging

Sequence Development

Clinical Knowledge

Biostatistics

Methods Validation

Methods Analysis

Computational Knowledge

MR Physics
Sequence Development

Clinical Knowledge

Biostatistics

Methods Validation

Image Analysis Methods

Computational Knowledge

MR Physics

Scanner with standard sequences

Correlative Studies and Hypothesis Testing

Image Analysis Tools and Collaboration

3rd Methods in International NeuroAIDS Research
Assessing Your MRI Capabilities

Define scanner: vendor, operating system, hardware, field strength (≥ 1.5T) (e.g., GE Signa Excite 3T Short Bore)

Head coil availability: 8-, 16- or 32-channel

Modality capabilities: anatomical; spectroscopy; diffusion tensor; echo planar imaging

Sequence capabilities: available standard sequences T1, T2, PD, FLAIR; and research possibilities

Image processing capabilities and collaborative options
Anatomical Image Analysis Methods

Segmentation for gray, white, & ventricular CSF:
  --FSL FAST
Probabilistic labeling
  --FreeSurfer or FSL FIRST
Cortical thickness
  --FreeSurfer

Segmentation for gray, white, ventricular and sulcal CSF, & cranial vault:
  --FSL FAST
  --Multi-channel
  --White matter abnormalities
Spectroscopy and Diffusion Image Analysis Methods

LC Model
--Provencher, 2001

FMRIB’s Diffusion Toolbox / FSL TBSS

Fiber Tract Mapping
--DTI Studio
Resources

HIV Neurobehavioral Research Center (HNRC) International Core supports consultation for exploring neuroimaging capabilities.

Supported by:
HIV Neurobehavioral Research Center (HNRC) P30MH062512
CNS HIV Anti-Retroviral Therapy Effects Research (CHARTER) Neuroimaging Core NIH HHSN271201000027C
NINDS R21 NS069355

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- FSL FIRST http://www.fmrib.ox.ac.uk/fsl/first/index.html
- Multi-channel and white matter abnormalities
  Jernigan et al. J. Neurovirology 2011
- LC Model  http://s-provencher.com/pages/lcmodel.shtml
- FSL TBSS  http://fsl.fmrib.ox.ac.uk/fsl/tbss/
- DTI Studio https://www.mristudio.org/