



Methods in International NeuroAIDS Research Conference
Frascati, Italy 2011

3rd Methods in International NeuroAIDS Research

July 14-16, 2011 | Frascati (Rome), Italy



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?

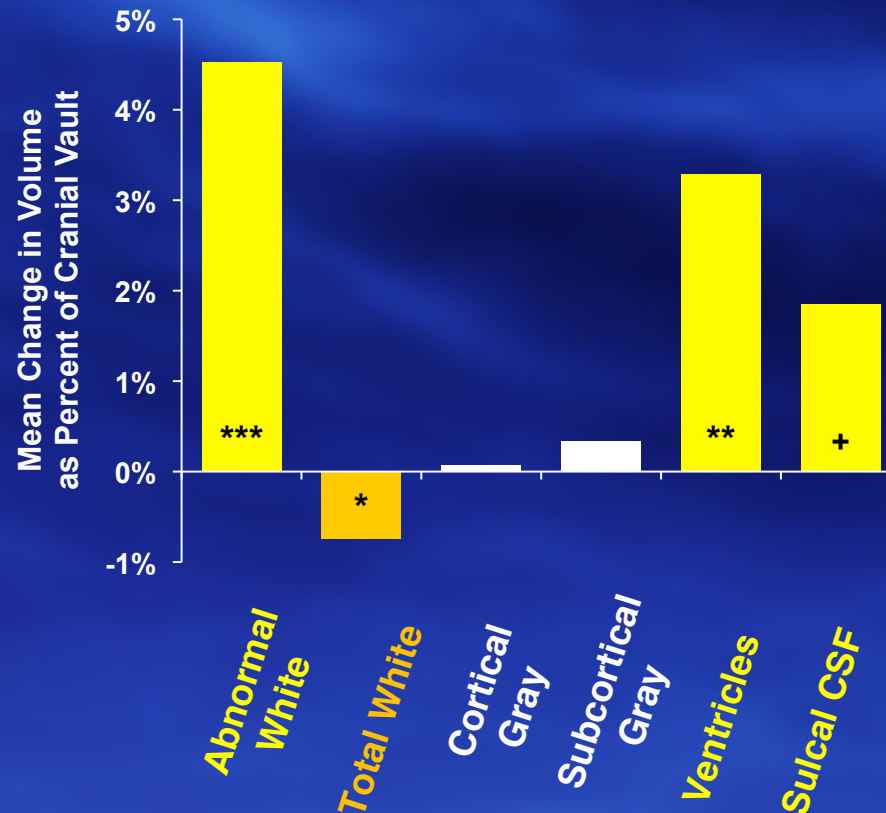
How does the brain respond during immune recovery, and does this impact cognition or functional performance?

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



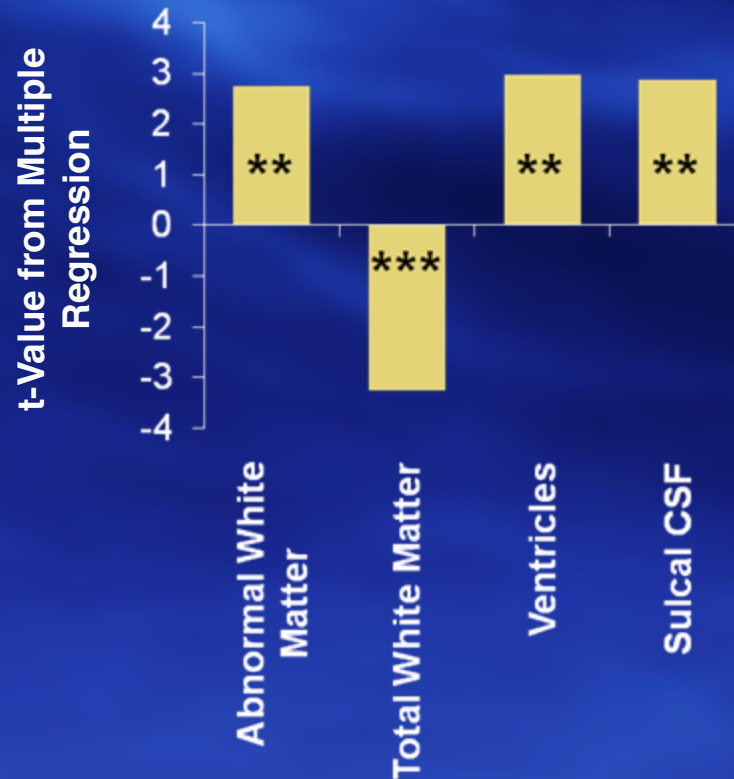
- Simple description of change over one year

Fennema-Notestine, preliminary CHARTER



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Lower Nadir CD4 and Structural Damage



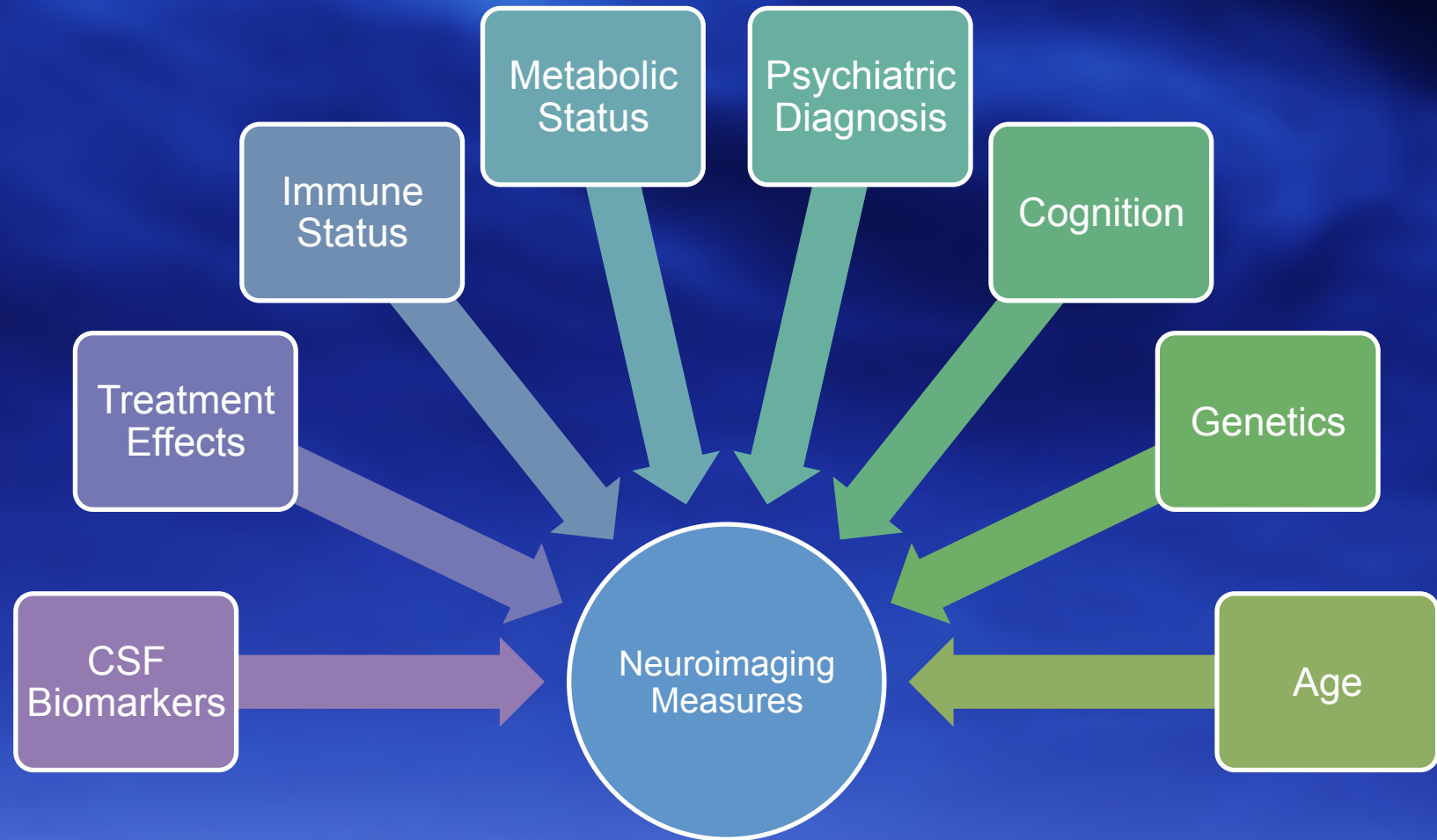
- Must consider multivariable models



Jernigan et al. 2011

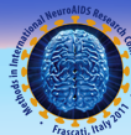
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Factors Associated with Brain Alterations

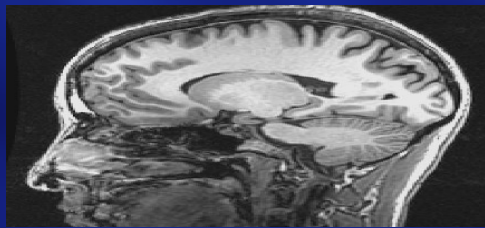


Common MRI Modalities

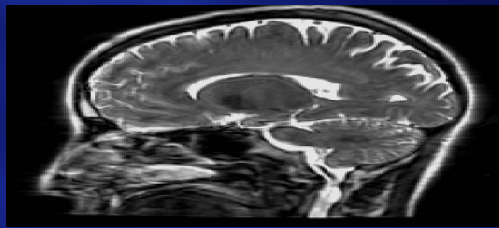
- Anatomical / Structural MRI
 - » Size of neuroanatomical structures and volume of CSF spaces provide indices of tissue damage, loss, and inflammation
- MR Spectroscopy
 - » Samples metabolite levels to assess neuronal integrity and inflammation
- Diffusion Tensor Imaging
 - » Integrity of white matter fibers



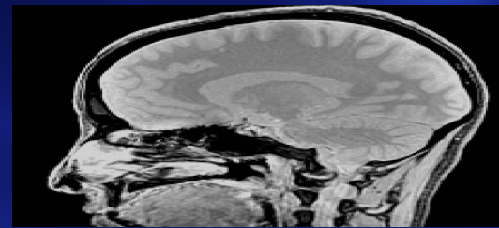
Anatomical



T1

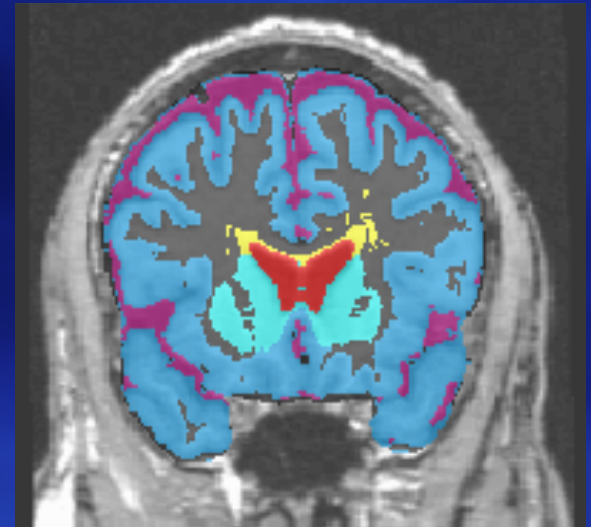
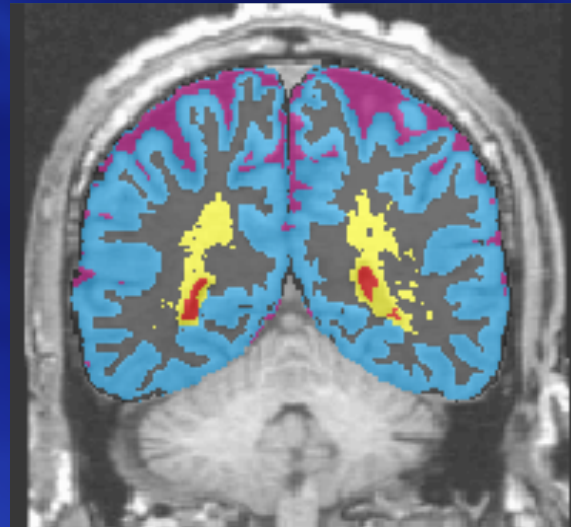
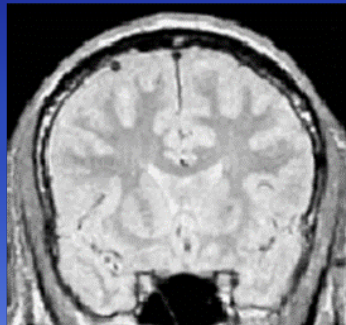
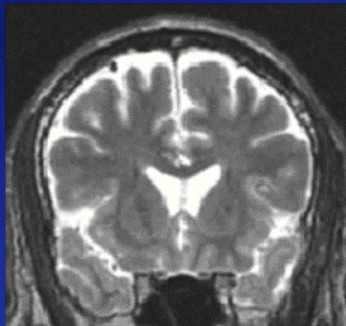
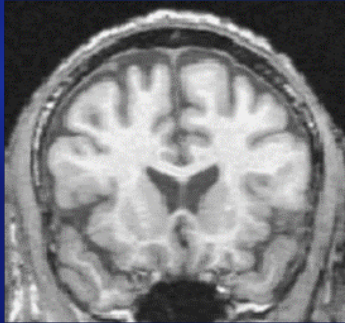


T2



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

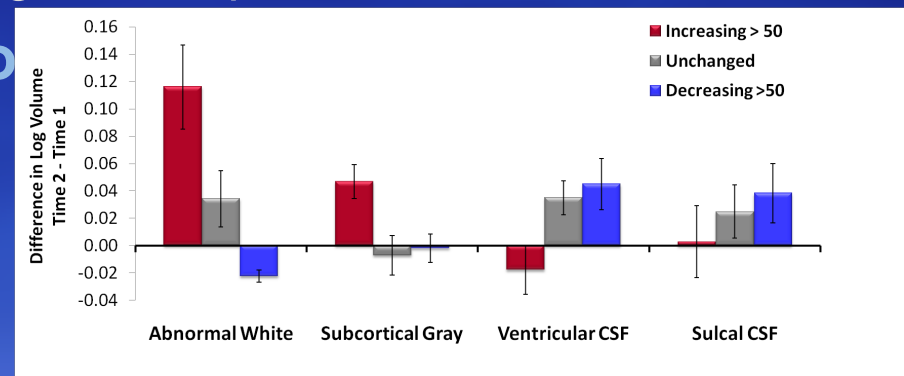
■ White matter pathology

- » 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

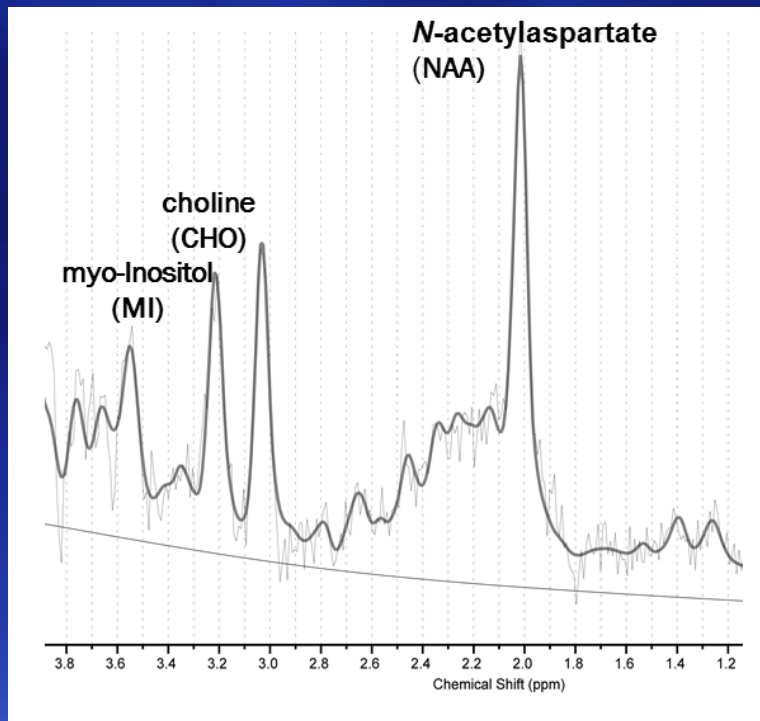


Fennema-Notestine et al. 2011

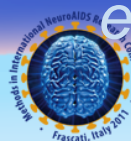


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MR Spectroscopy Metabolites

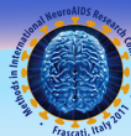
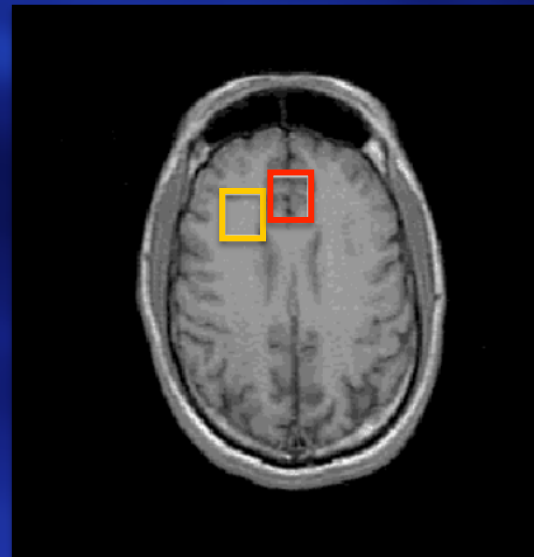
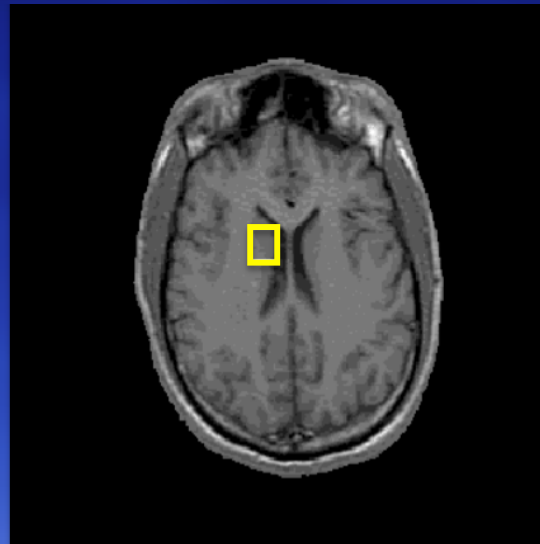


- *N-acetylaspartate (NAA): neuronal integrity*
- *Choline/choline-containing compounds (Cho): cell membrane degradation and lipid changes*
- *Myo-inositol (MI): glial proliferation / inflammation*
- *Creatine/phosphocreatine (Cr): energy stores*



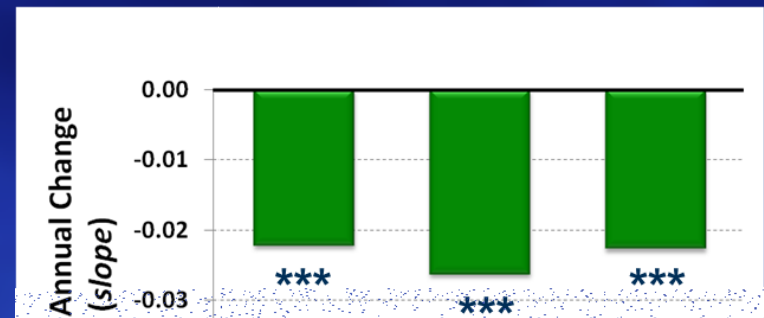
Common regions of interest in HIV

- 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



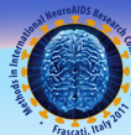
Fennema-Notestine, Taylor et al., preliminary CHARTER



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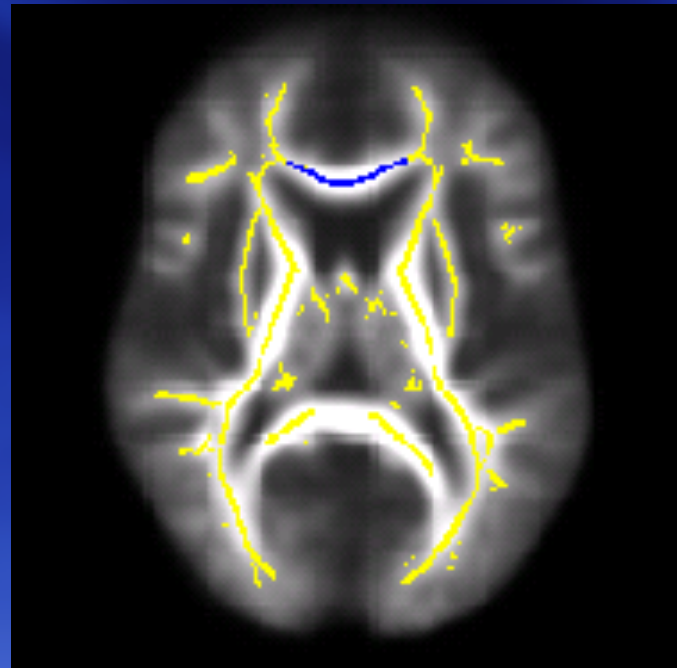
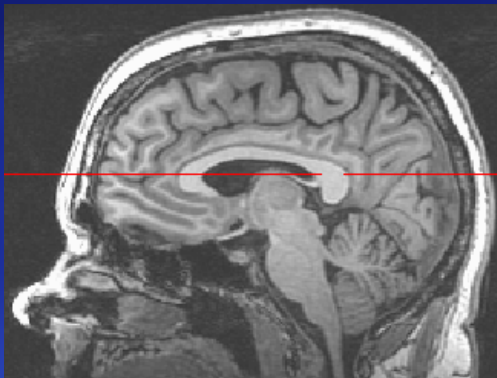
Diffusion Tensor Imaging (DTI)

- 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

What are the common characteristics of neuropathogenesis in the current era?

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

Is history of severe immunosuppression (CD4 nadir) associated with tissue damage or loss?

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

How does the brain respond during immune recovery, and does this impact cognition or functional performance?

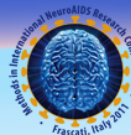
- Suggestions of inflammation in white matter and subcortical gray are being explored in association with cognition.

Does the combination of HIV and a psychiatric disorder increase the likelihood of brain injury?

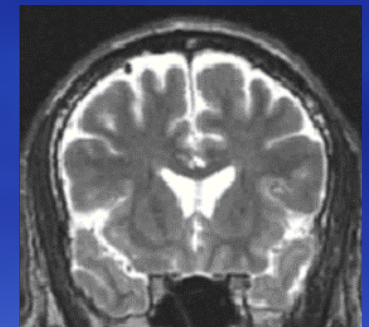
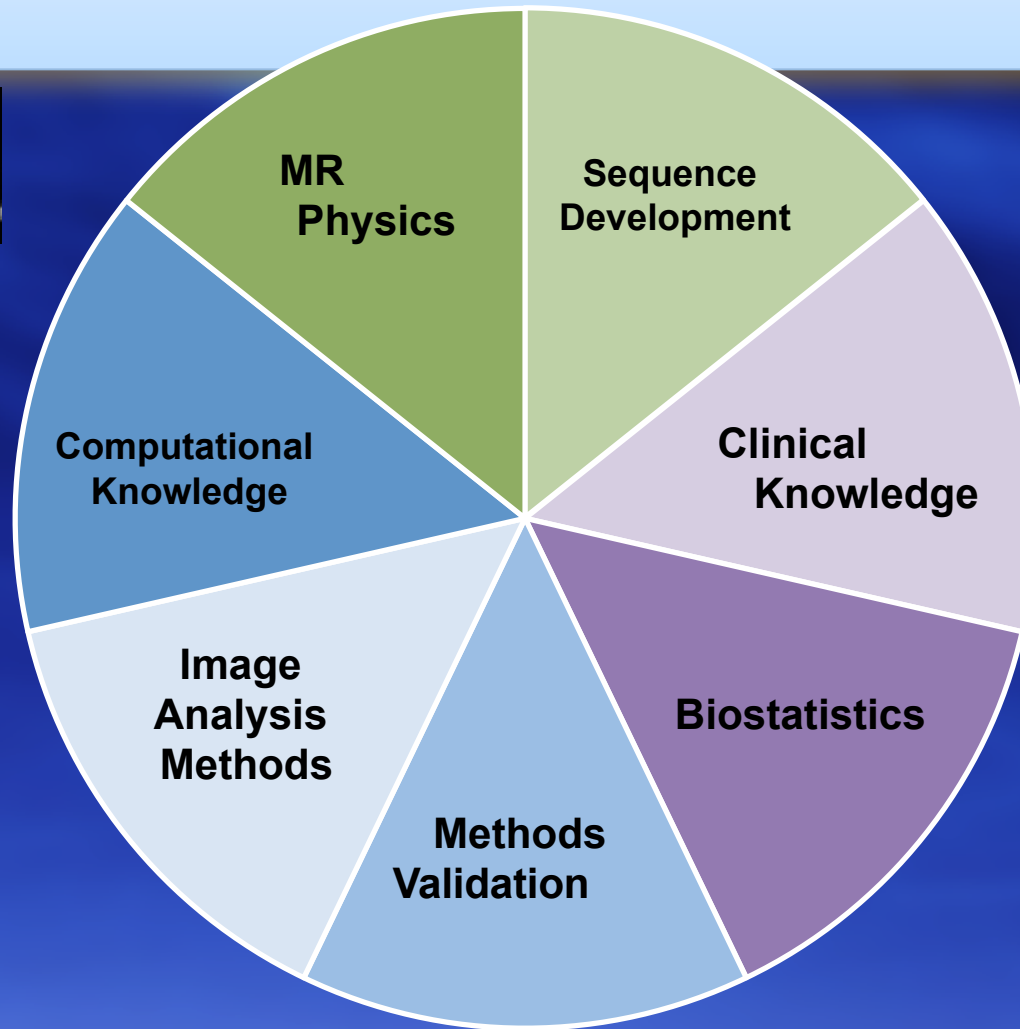
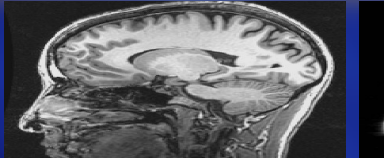
- Studying whether history of severe trauma influences presentation of HIV in the brain (*S. Seedat, South Africa*).

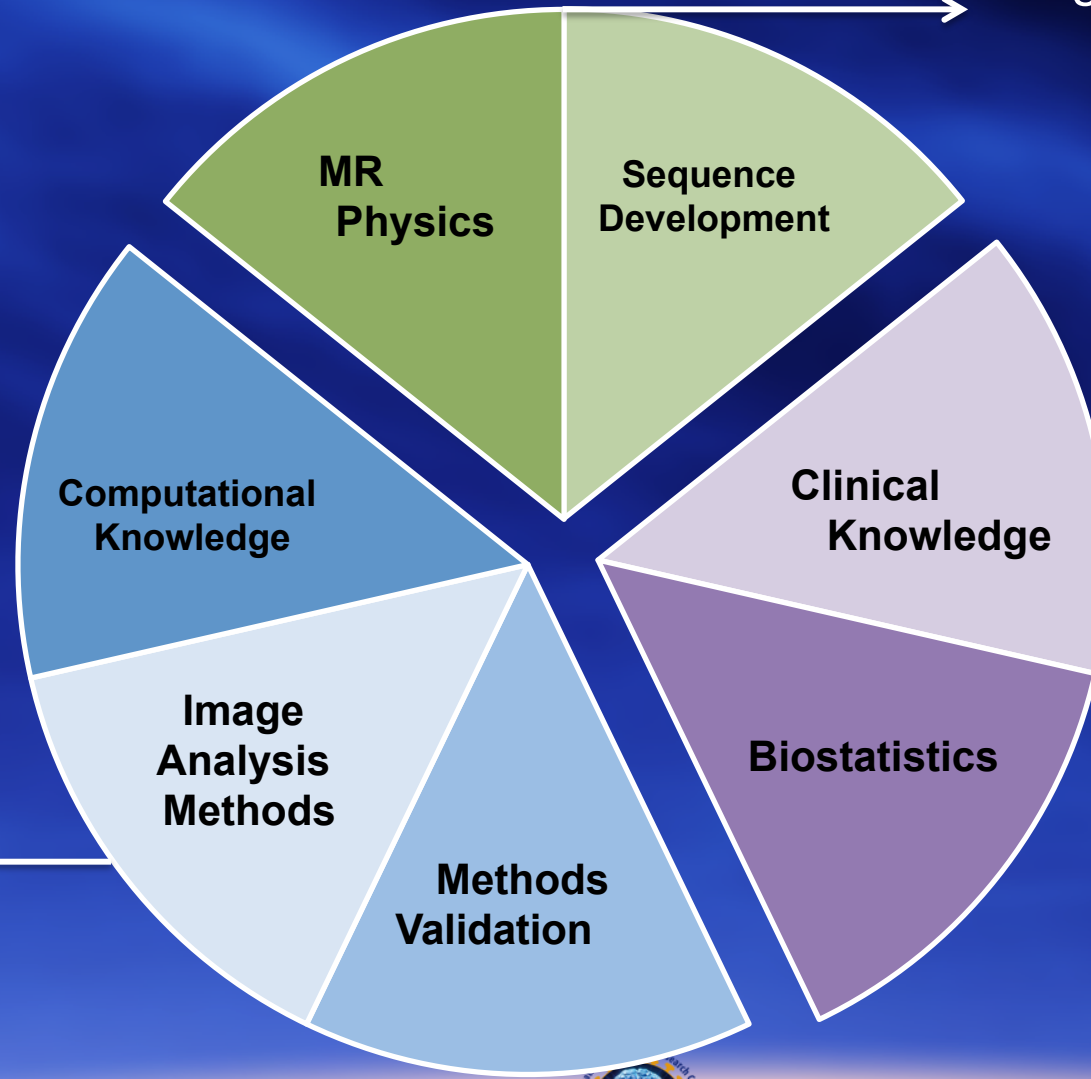
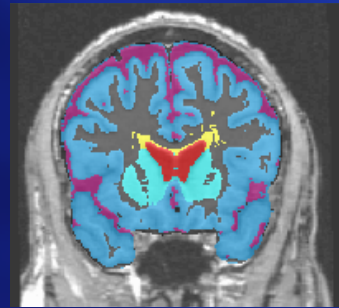
Can patterns of abnormalities classify individuals at greatest risk for cognitive decline?

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



Magnetic Resonance Imaging





Scanner with standard sequences



Image Analysis Tools and Collaboration

Correlative Studies and Hypothesis Testing



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Assessing Your MRI Capabilities

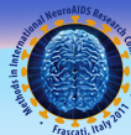
Define scanner: vendor, operating system, hardware, field strength ($\geq 1.5\text{T}$)
(e.g., *GE Signa Excite 3T Short Bore*)

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

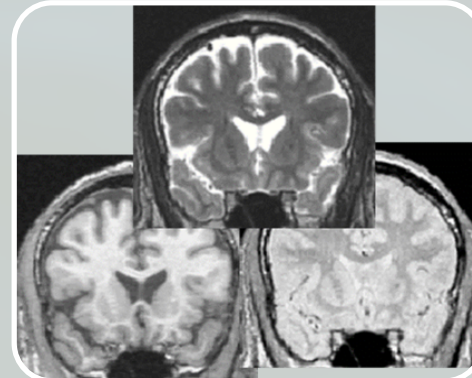
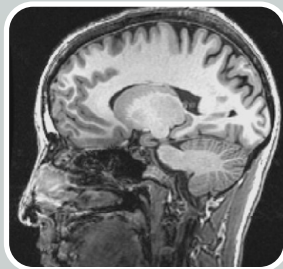
Modality capabilities: anatomical; spectroscopy; diffusion tensor; echo planar imaging

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

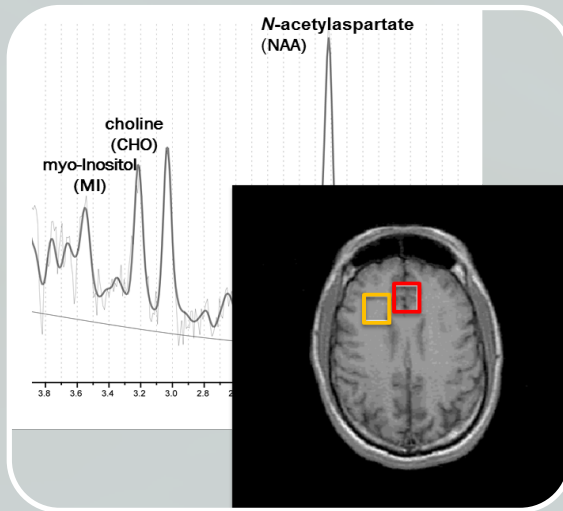
--FSL FAST

--Multi-channel

--White matter abnormalities

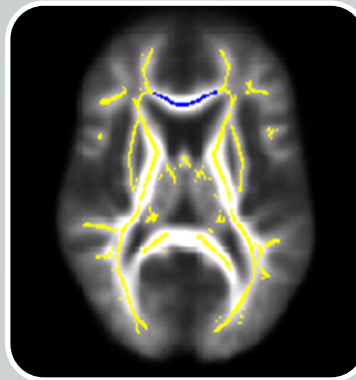


Spectroscopy and Diffusion Image Analysis Methods

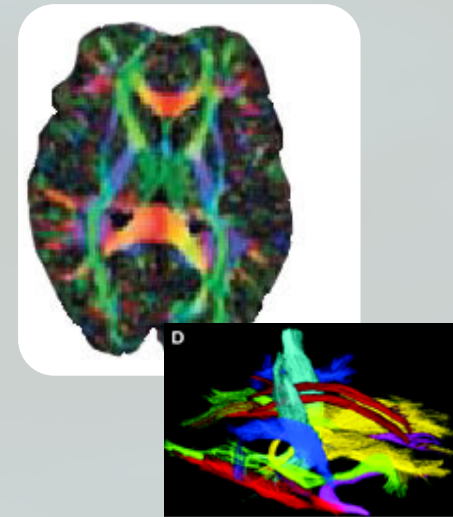


LC Model

--Provencher, 2001



FMRIB's Diffusion
Toolbox /
FSL TBSS



Fiber Tract
Mapping

--DTI Studio



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Resources

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

Supported by:

HIV Neurobehavioral Research Center (HNRC) P30MH062512

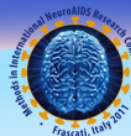
CNS HIV Anti-Retroviral Therapy Effects Research (CHARTER)

Neuroimaging Core NIH HHSN271201000027C

NINDS R21 NS069355

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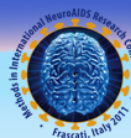


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Methods References

- FSL FAST <http://www.fmrib.ox.ac.uk/fsl/fast4/index.html>
- FreeSurfer <http://surfer.nmr.mgh.harvard.edu/fswiki>
- 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/>





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