Driving Biological Problem Huntington's Disease

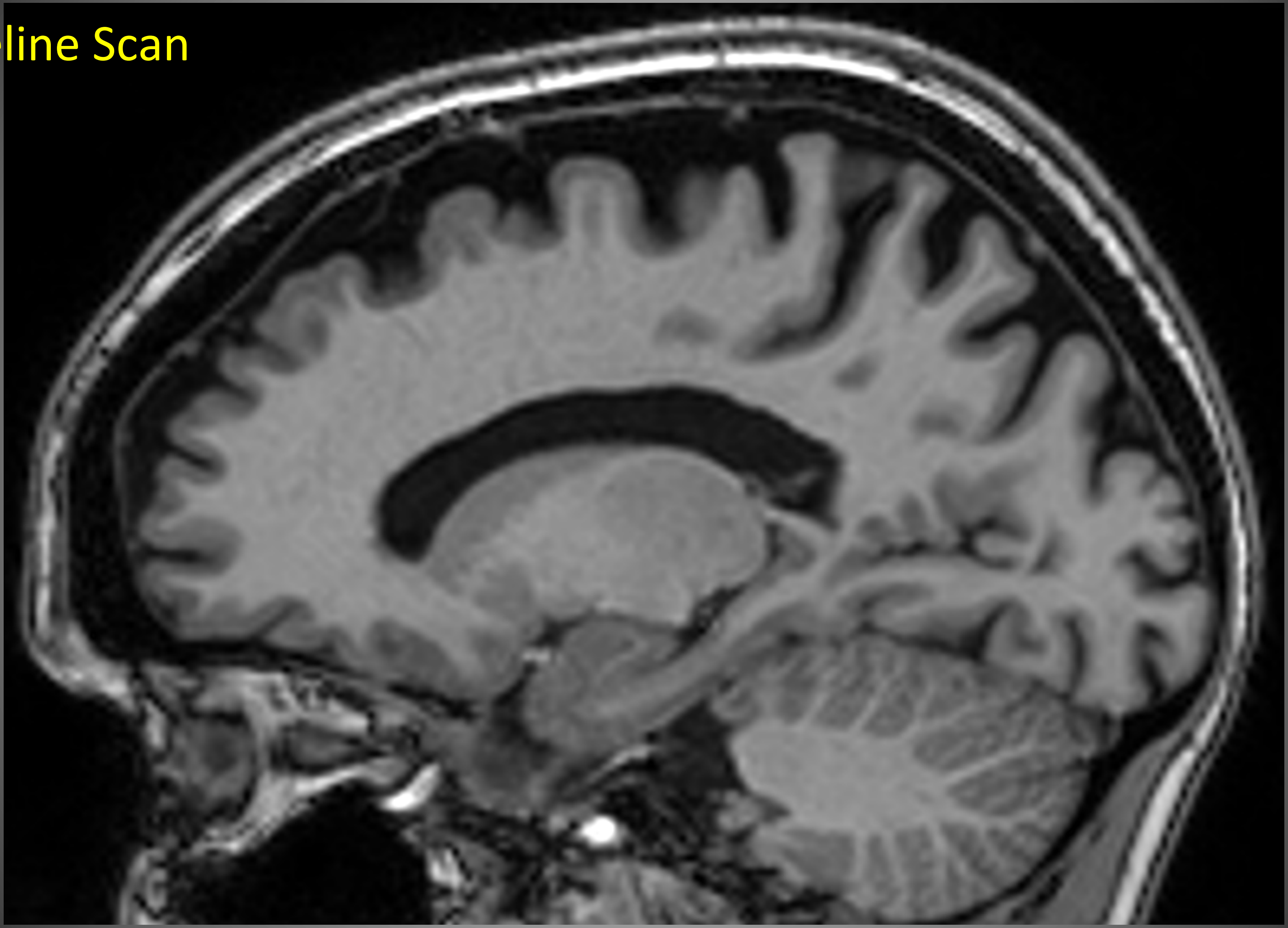
The University of Iowa

Builds on PREDICT-HD

The NIH-funded project "Neurobiological Predictors of Huntington's Disease" (PREDICT-HD) studies Huntington's disease (HD), a neurodegenerative genetic disorder that affects muscle coordination, behavior, cognitive function, and causes severe debilitating symptoms by middle age.

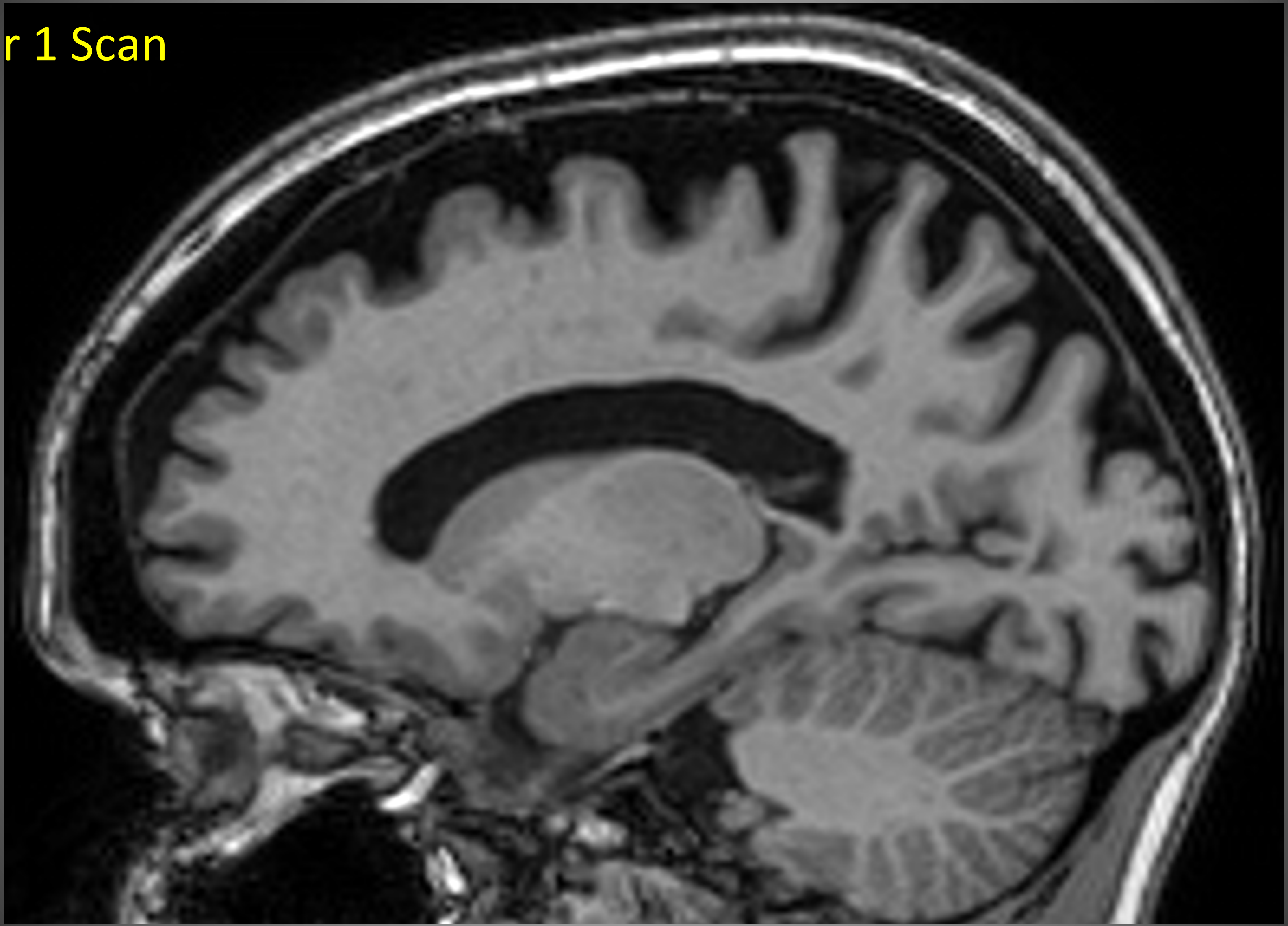
TRACK-HD Stage 1 HD Subject

Baseline Scan

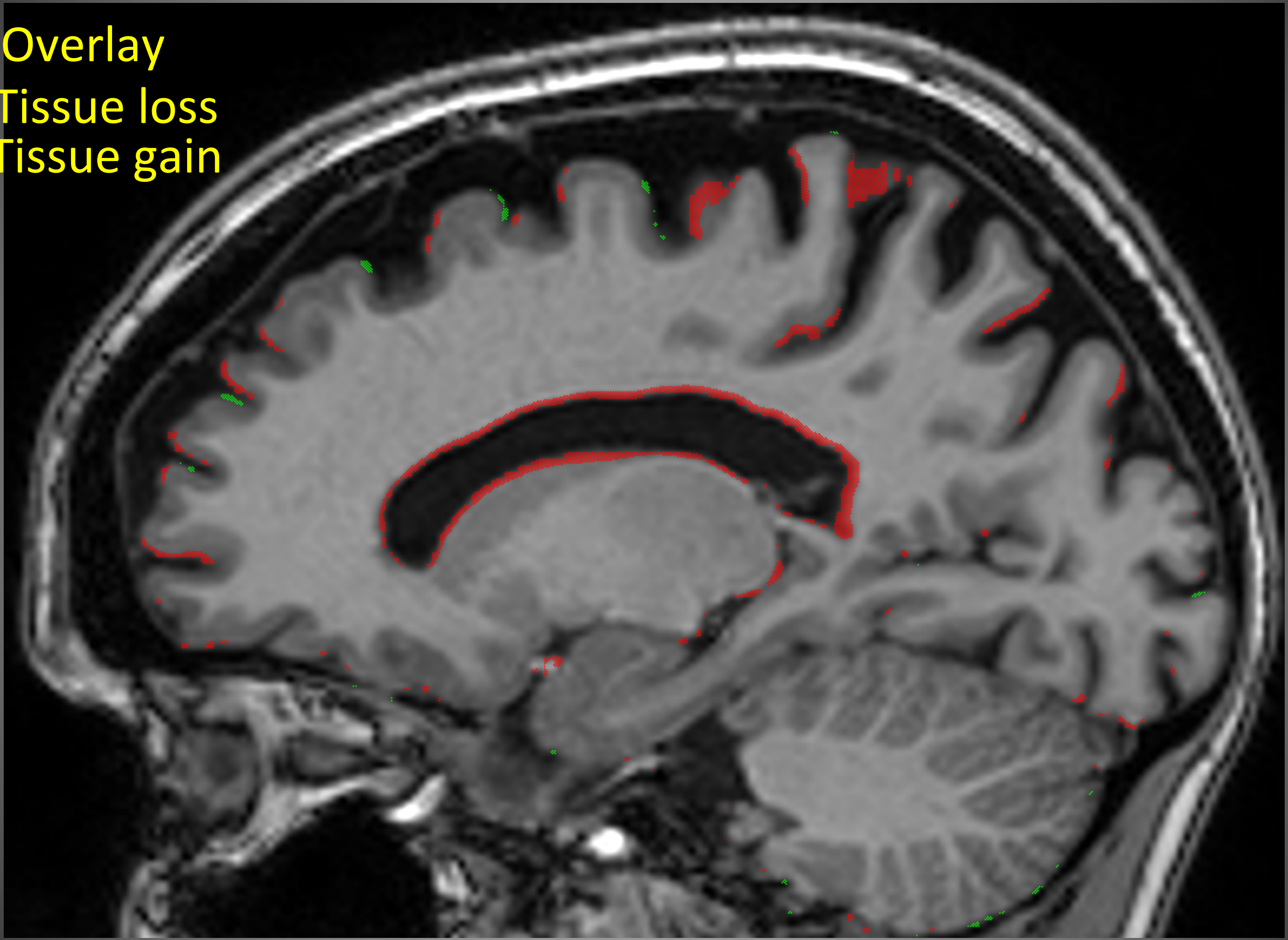


TRACK-HD Stage 1 HD Subject

Year 1 Scan

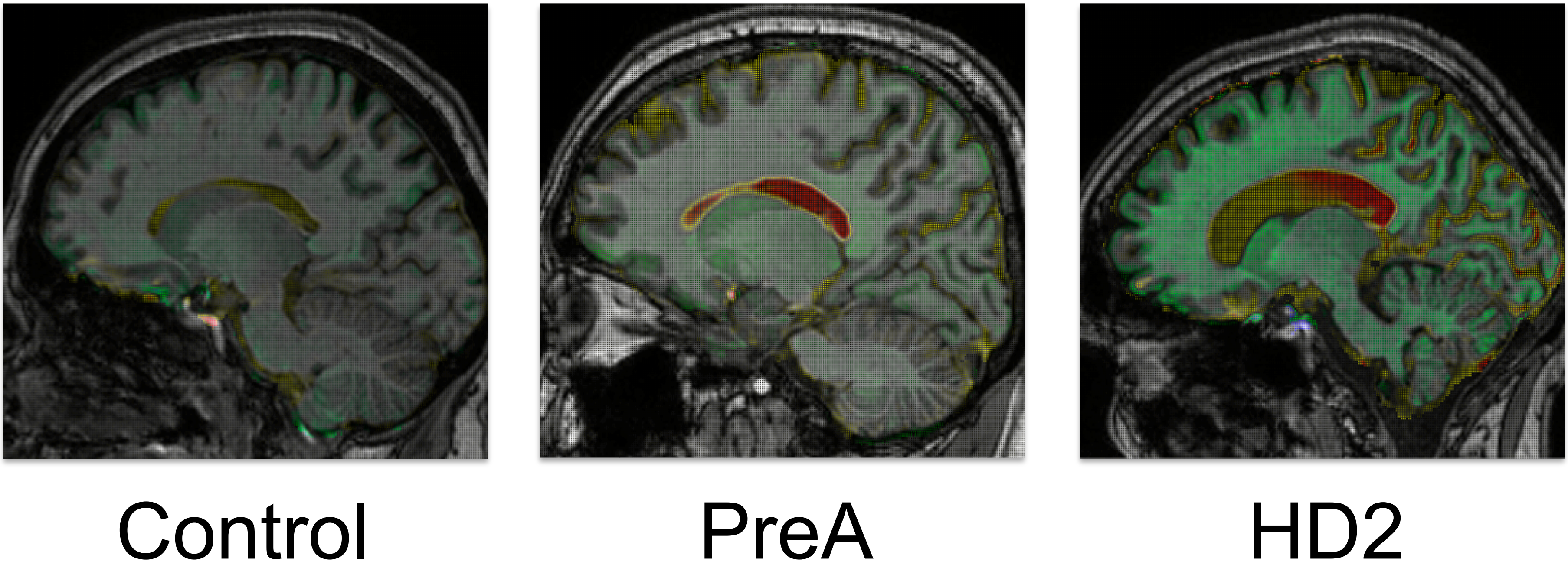


TRACK-HD Stage 1 HD Subject

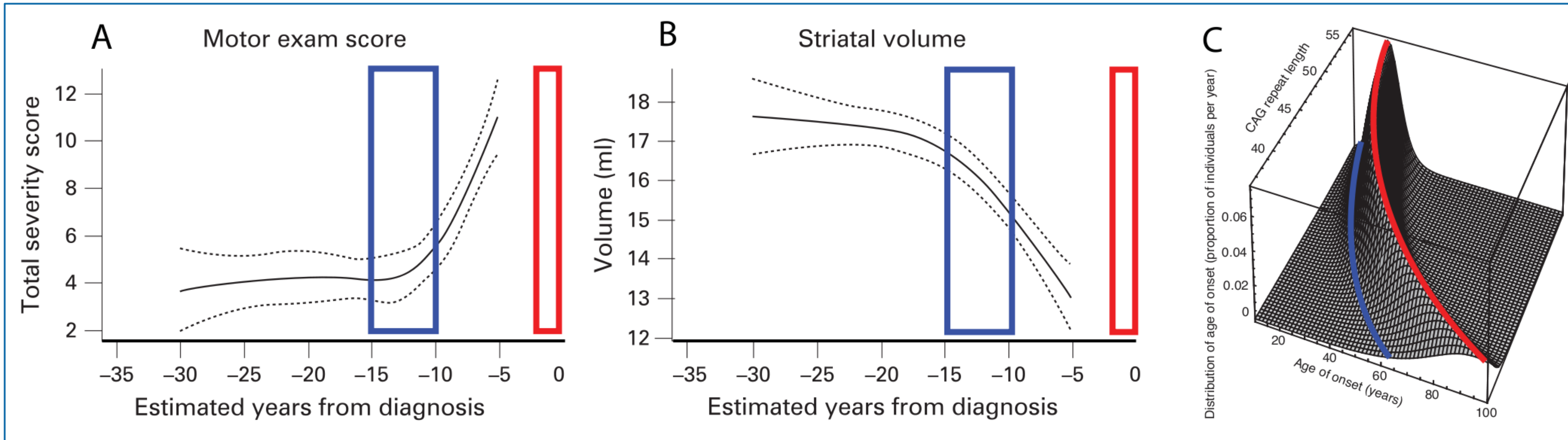


Atrophy Rate: 1.9% Premanifest Rate: 0.7% Control Rate: 0.2%

24-month voxel-compression mapping

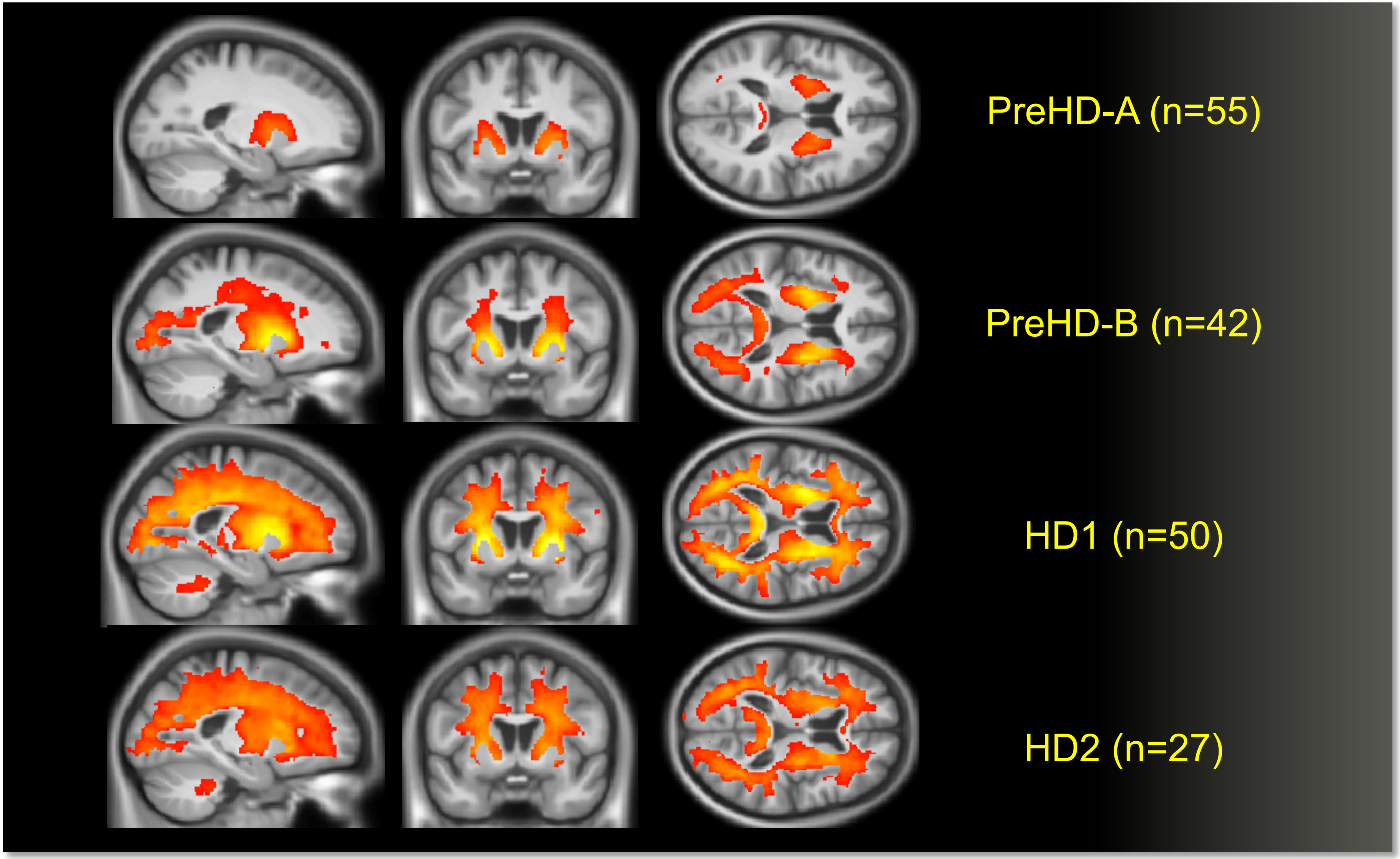


HD Background



The relationship between estimated years to diagnosis of HD and motor exam score and striatal volume (A,B). Distribution of age of onset for subjects with 36-56 GAC repeats (C). Red box indicates most likely time of diagnosis, blue box is the proposed time that intervention would have the greatest impact.

Change in White Matter vs Controls (n=96)



Specific Aims

- Perform individualized longitudinal shape change quantification from multi-modal data.
- Complete full brain Diffusion Tensor Imaging tractography analysis.
- Deploy extensible tools for sharing source data, derived data, algorithms and methods to multi-site analysis teams.

Methods: Aim 3.

- Deploy the XNAT environment.
- Extend the NA-MIC data-sharing tools to disseminate raw scan data, derived datasets, and measurement scores for Aims 1 and 2.
- Incorporate existing morphometric analysis pipelines into XNAT.

Sharing HD Data

http://www.na-mic.org/Wiki/index.php/2011_Summer_Project_Week

Data Files

- File:Anonymized factorsExternalIDs with blage mriDate scanID daysSince.xlsx
- File:NAMIC+Factors.doc
- File:NAMIC HD DWI DTI.xlsx
- File:NAMIC HD DataDescription.pdf
- File:ANN Segmentation thesis.pdf
- File:20111102 ANNSegmentation.pptx

Subjects SELECT

<< first < prev 1 2 3 4 5 next > last >> 20 1 of 6 Pgs (115 Rows) Reload Options

Subject	M/F	Hand	YOB	MR Sessions
10001	U	U		6
10002	U	U		6
10003	U	U		6
10004	U	U		6
10005	U	U		4
10006	U	U		6
10007	U	U		4
10008	U	U		5
10009	U	U		6
10010	U	U		6
10011	U	U		6
10012	U	U		8
10013	U	U		6
10014	U	U		6
10015	U	U		8
10016	U	U		6
10017	U	U		6

Shared Sites (14 labs)

CSAIL

THE UNIVERSITY OF UTAH

HARVARD MEDICAL SCHOOL

Georgia Institute of Technology
School of Electrical and Computer Engineering
College of Engineering

Florida State University
Tallahassee, Florida 32306-4330
Department of Statistics
(850) 644-3218

MAX-PLANCK-GESELLSCHAFT

BRIGHAM AND WOMEN'S HOSPITAL

Currently Shared Data

- Anonymized Raw Scan data
- Derived Data

ELSEVIER

NeuroImage

Volume 54, Issue 1, 1 January 2011, Pages 328–336

Fully automated analysis using BRAINS: AutoWorkup

Ronald Pierson[a], Hans Johnson[a], Gregory Harris[a], Helen Keefe[a], Jane S. Paulsen[a, c], Nancy C. Andreasen[a], Vincent A. Magnotta[b]

Improving shared derived data processing

Documentation-Rons-Rules-For-Tools

Documentation-Rons-Rules-For-Tools

Introduction

"Rules for tools" is an informal set of rules that developers should keep in mind when working on **interactive tools** for translational clinical research. If you follow them, you will create tools that many people will use.

1. You make it, I break it. [1]
2. Your tool does not exist, until it works on my laptop with my data. [2]
3. I am lazy. I do not like to move the mouse or to type. [3]
4. No more than one simple parameter. [4]
5. I have ADD. Make your algorithm fast. [5]

HOW TO MAKE ALGORITHMS ROBUST

- Build a case library with 10 or more cases
- Use half for development, cycle through the cases daily
- Use the other half for testing

Improving shared derived data processing

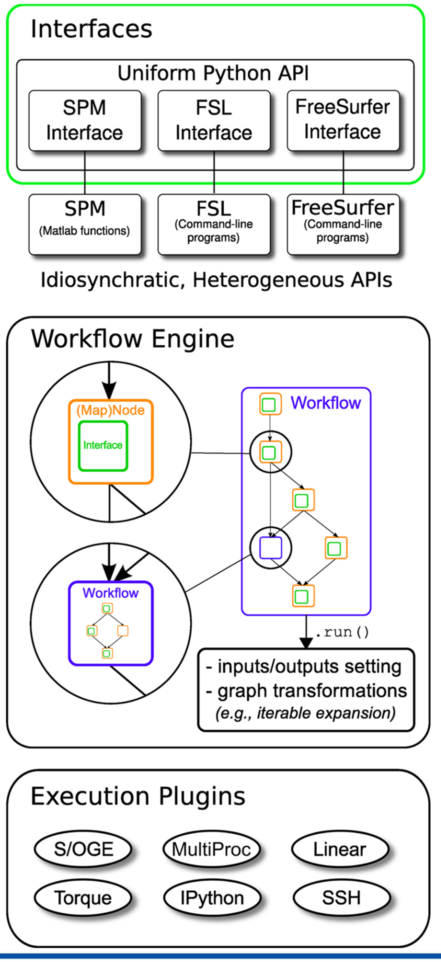
- Convert brains2 internal tools auto workup into fully NA-MIC compliant tool suite
  - Convert major applications to SEM compliance (Decouple SEM from Slicer)
  - Use SimpleITK to replace brains2 basic image processing building blocks
  - Transition Slicer to ITKv4 (Thanks Bill Lorensen)
  - Define workflows in NiPype (Thanks Satra Ghosh)

NiPype Key Features

- Naïve Approach
  - Smooth, denoise, etc.
  - Mask brain
  - Register to Atlas
  - …
- Better Approach

  Some images have noticeable field bias
  - Insert N4 bias correction step

NiPype: Large catalog of tools with a uniform interface



- **Batch processing**
  - Distributed processing plugins
  - Reruns affect updated/edited node connections ONLY!
- Uniform node creation
  - Stable API
  - Nipype's Function node allows easy integration of CLI tools
- **Pipeline complexity**
  - Iterables, MapNodes
  - Nested workflows

Image source: Gorgolewski K *et al.,* (2011) Nipype: a flexible, lightweight and extensible neuroimaging data processing framework in Python. Front. Neuroinform. 5:13.

NiPype: Can be seamlessly integrated With many of the other NA-MIC tools

```
import regexNode, n4correct  # Scripted modules
import BRAINSFit             # Nipype API wrapped module
import nipype.pipeline.engine as pe
from nipype.interfaces.utility import Function, IdentityInterface

registration = pipe.Workflow(name = "registration")

filesNode = pe.Node(name = "filesNode", IdentityInterface(fields = ["filename"]))
filesNode.iterables = ("filename", inputFiles)

regexNode = pe.Node(name = "regexNode", Function(function = fileRegex,
                                                 input_names = ["filename"],
                                                 output_names =["outputVolume","outputLabel"]))

n4bias = pe.Node(name = "N4BiasCorrection", Function(function = n4correct,
                                                     input_names = ["inputVolume",
                                                                    "labelVolume"],
                                                     output_names = ["outputVolume"]))
n4bias.inputs.convergenceThreshold = 0.0005
n4bias.inputs.bSplineOrder = 6

bFit = pe.Node( name = "BRAINSFit", interface = BRAINSFit())


...

registration.connect([(filesNode, regexNode, [("filename", "filename")]),
                      (regexNode, n4bias, [("outputLabel", "labelVolume"),
                                           ("outputVolume", "inputVolume")]),
                      (n4bias,    bFit,   [("outputVolume", "inputVolume")]) ])
```

Create the pipeline node

Connect the node

Methods: Aim 1

- Use shape analyses to create a normative model.
- Changes in an individual's scores can then be used to inform clinical counseling and intervention scheduling decades before a neurological motor diagnosis is made.

Timeline: Year 1

- Aim1: Apply preliminary tools for longitudinal shape change to existing data
- Aim2: Create a quality control pipeline of DTI datasets.
- Aim3: Deploy XNAT instance and populate with PREDICT-HD data

Brain Sub-Cortical Structures: BRAINSCut

Developed

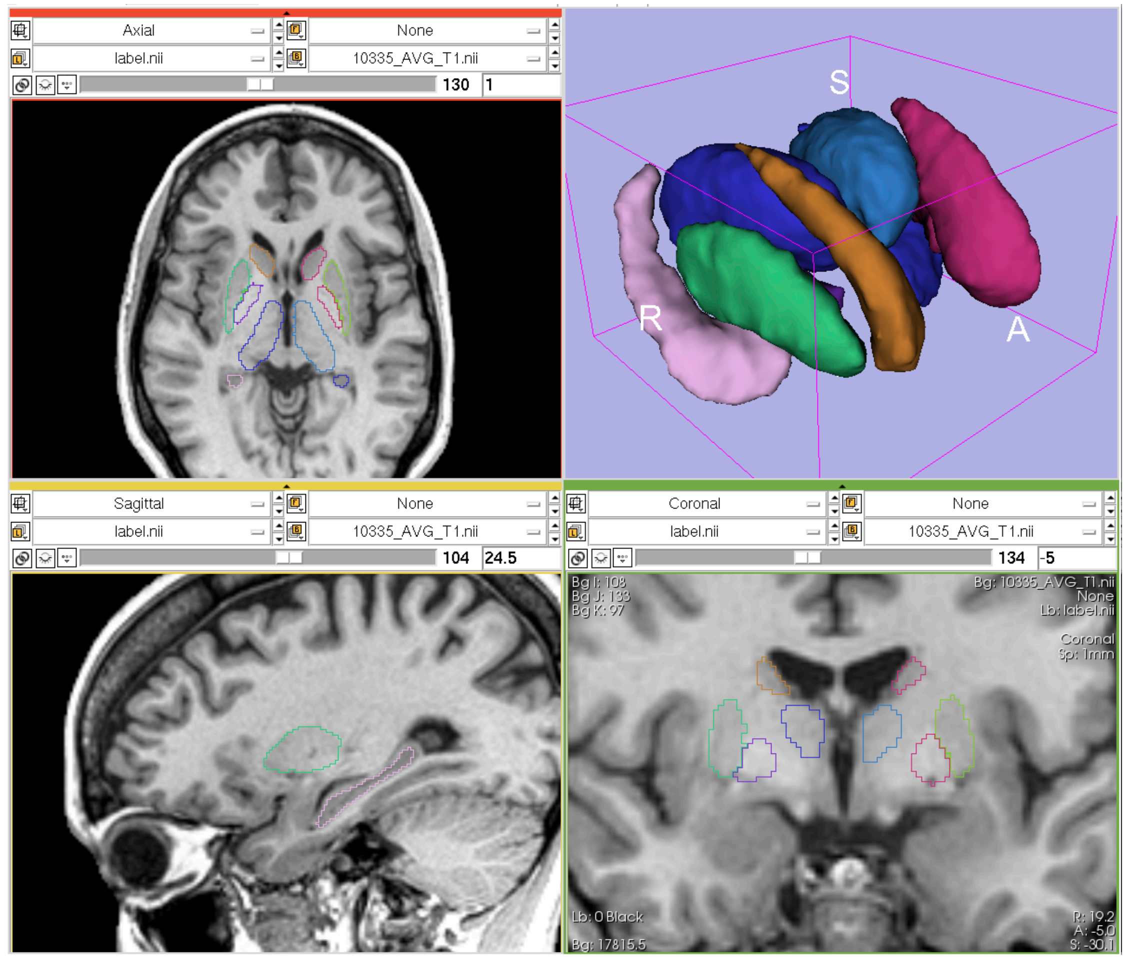
- Caudate
- Putamen
- Thalamus

New structure

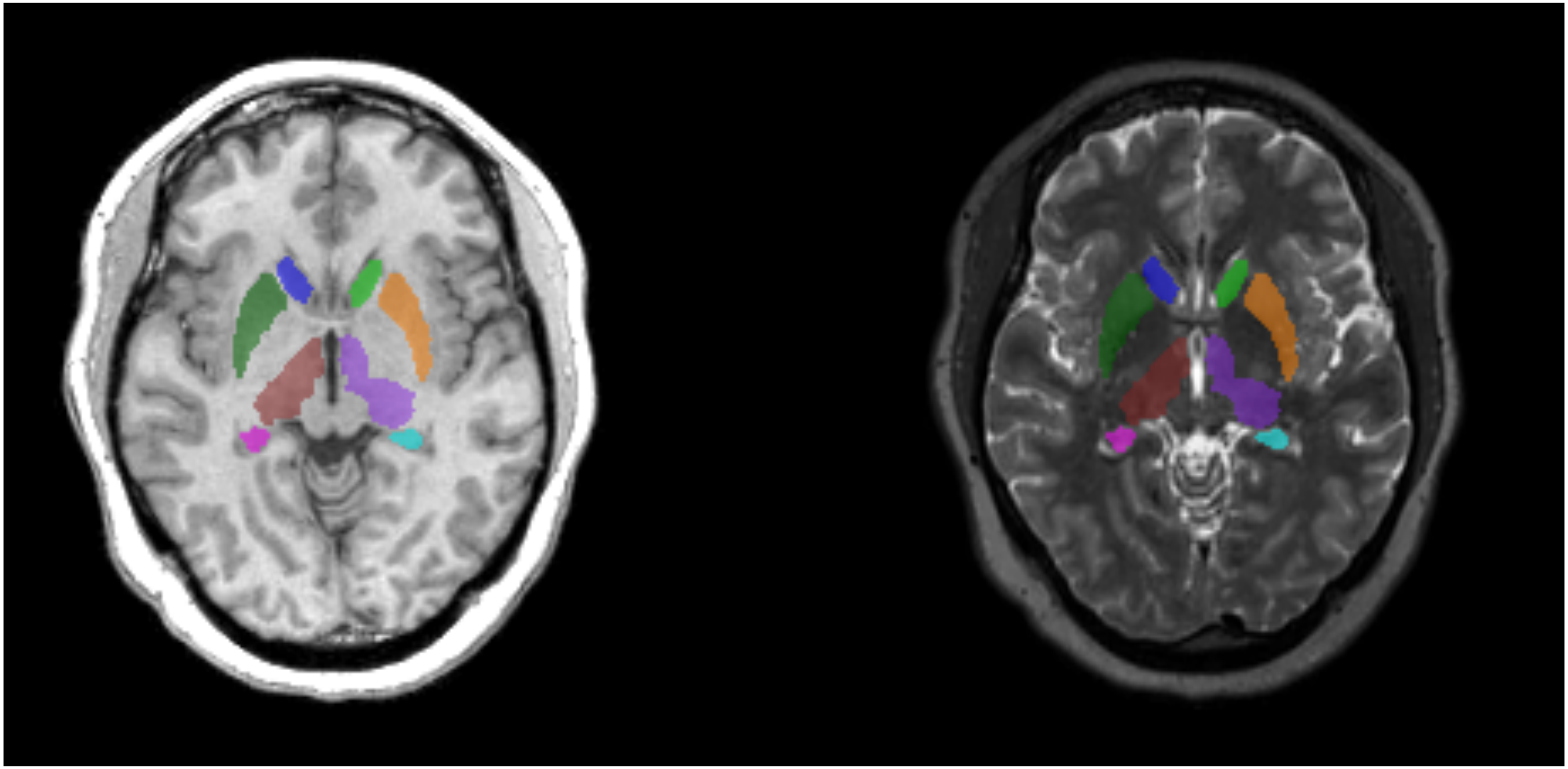
- Hippocampus

On going

- Globus
- Accumbens
- And more…



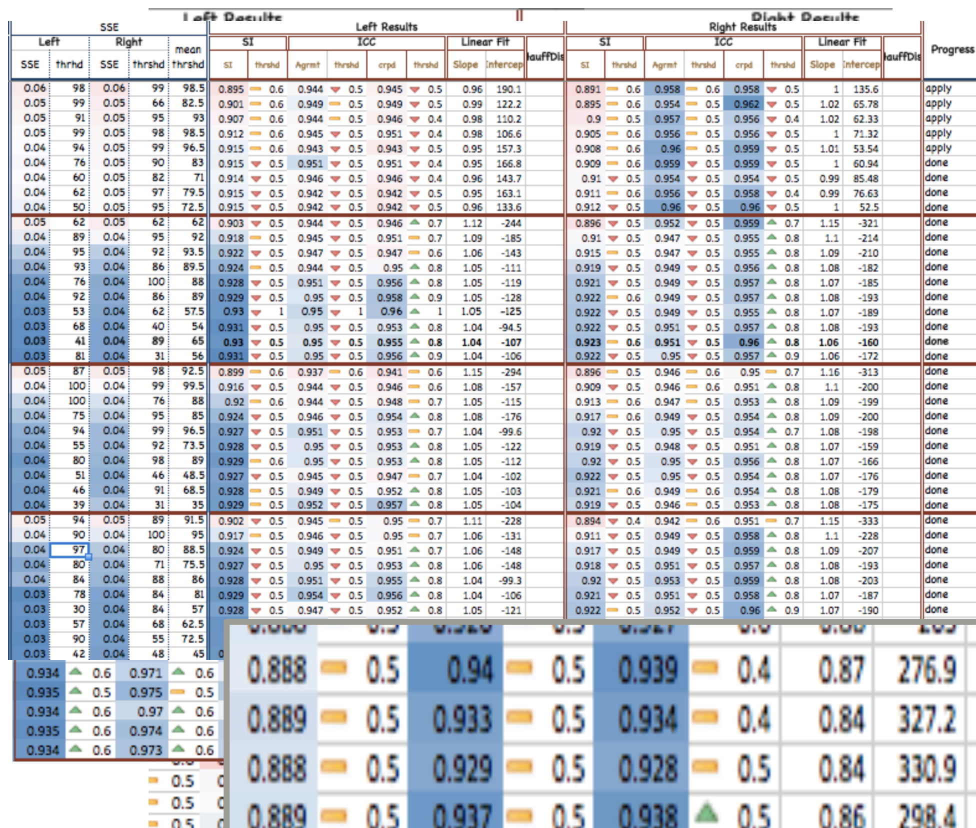
Sub-Cortical Structures: BRAINSCut: Detailed View



Brain Sub-Cortical Structures: BRAINSCut: Reliability

Testing data includes Multi-sites, which means:

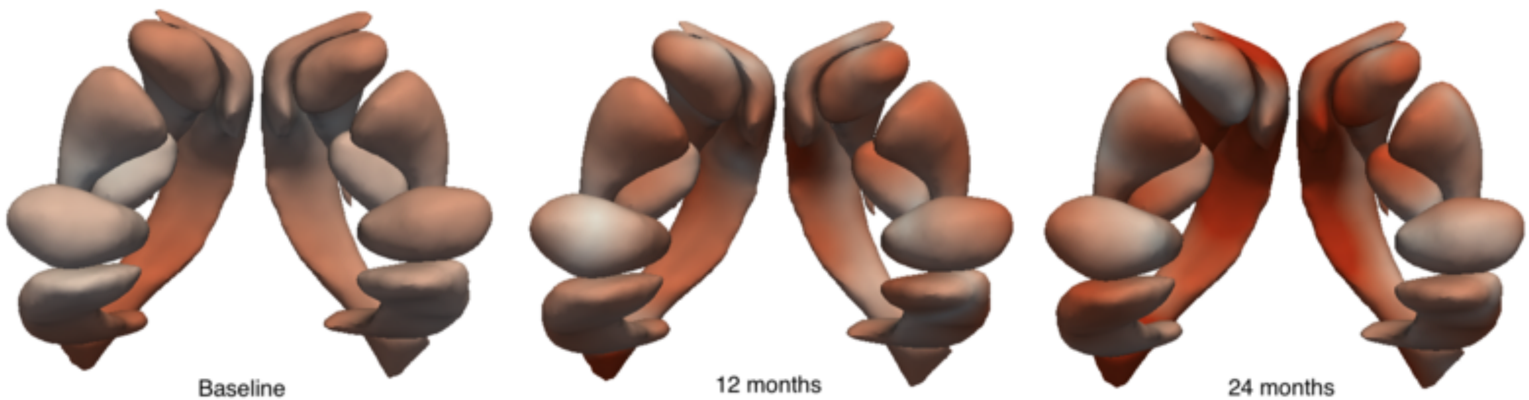
- Different protocols
- Variation of subjects!!!

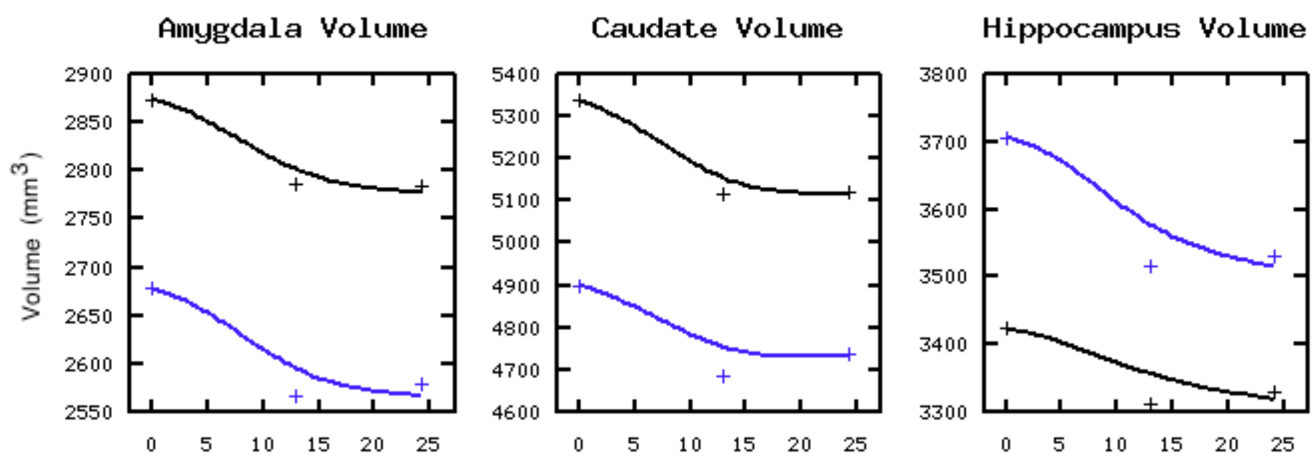


0.888	0.5	0.94	0.5	0.939	0.4	0.87	276.9
0.889	0.5	0.933	0.5	0.934	0.4	0.84	327.2
0.888	0.5	0.929	0.5	0.928	0.5	0.84	330.9
0.889	0.5	0.937	0.5	0.938	0.5	0.86	298.4

Intra class correlation ≈ 0.92~0.93

Longitudinal Shape





James Fishbaugh

Diffusion Data: Summary of Work

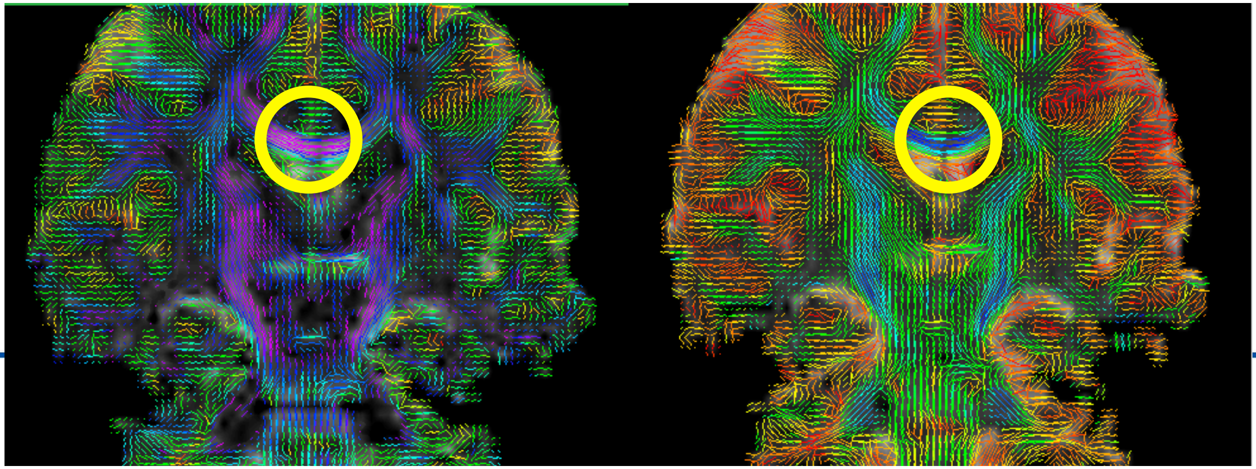
- Design image processing pipeline and longitudinal statistical analyses for large amounts of multi-site diffusion-weighted data
  - Data used: ~260 scan sessions
    - Collected at 2 PREDICT-HD sites
    - Cases and controls
    - Up to 4 data acquisitions at 1 year intervals
    - Included structural and clinical data
- Apply/extend pipeline and analyses to larger PREDICT-HD data set
  - Data that will be used: 813 scan sessions + ~13 new per week
    - Collected at 31 PREDICT-HD sites over
    - Cases and controls
    - Includes structural and clinical data

Diffusion Data: Completed Work

- Designed image pre-processing pipeline
  - Proper and consistent conversion of DICOM diffusion data to NRRD
    - DicomToNrrdConverter (Xiaodong Tao, UNC, Iowa)
  - Quality control
    - Manual visual inspection of raw DWI data (Iowa)
    - Removed bad data: DTIPrep (UNC)
- Designed techniques for extracting DTI scalar measurements from ROIs
  - Label statistics (SimpleITK)
  - Segmented preliminary ROIs: caudate, putamen, white matter by lobe

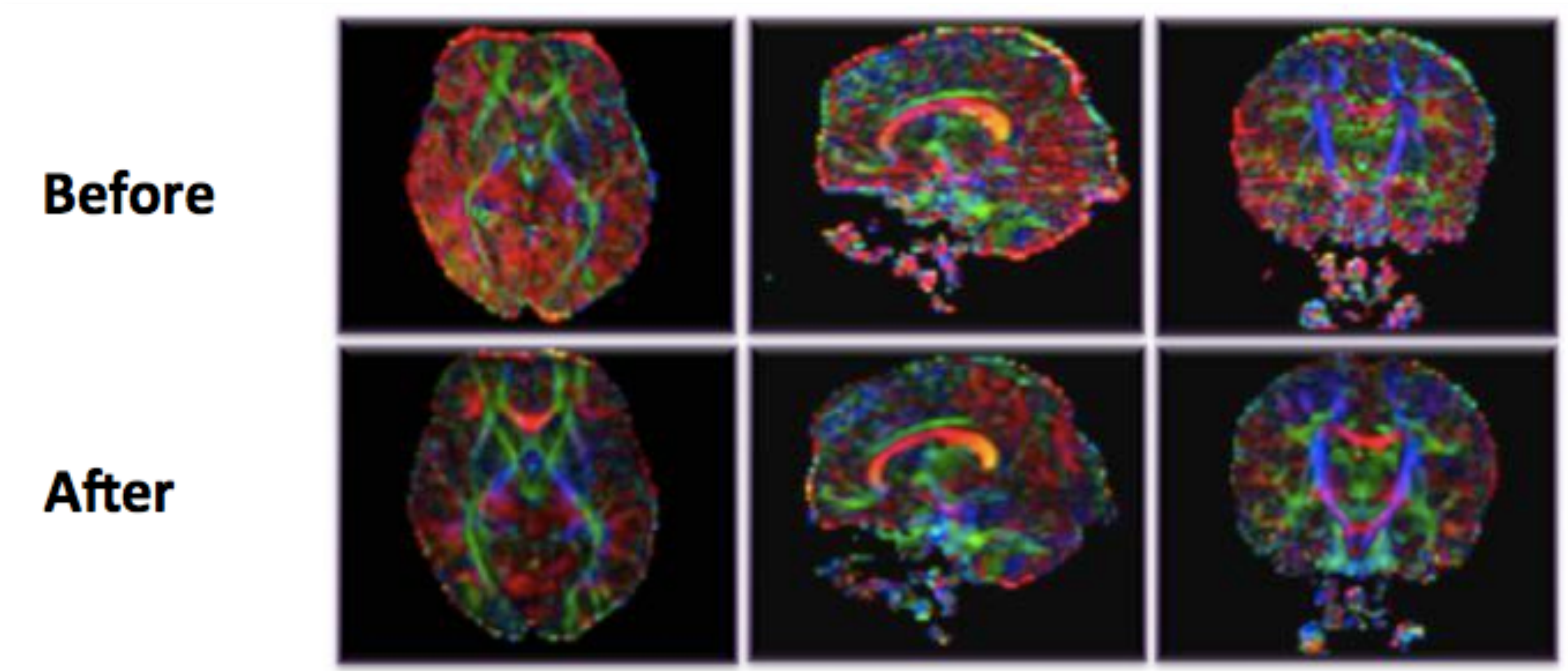
Proposed Pipeline: DicomToNrrdConverter

- Properly converts DICOM data to NRRD files for 12 types of data (Siemens, Philips, and GE)
- Back-calculates diffusion-sensitizing gradient coordinates from **b** matrix when coordinates are incorrect in DICOM header

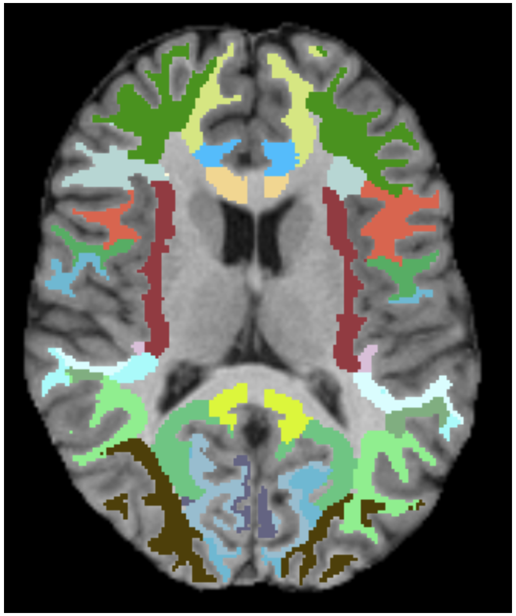


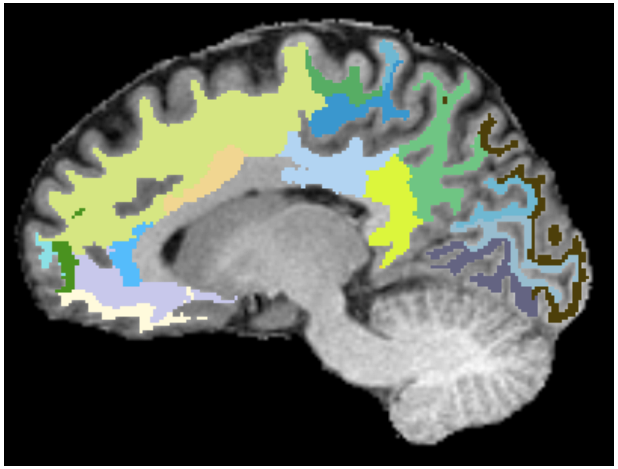
Diffusion Data: Completed Work

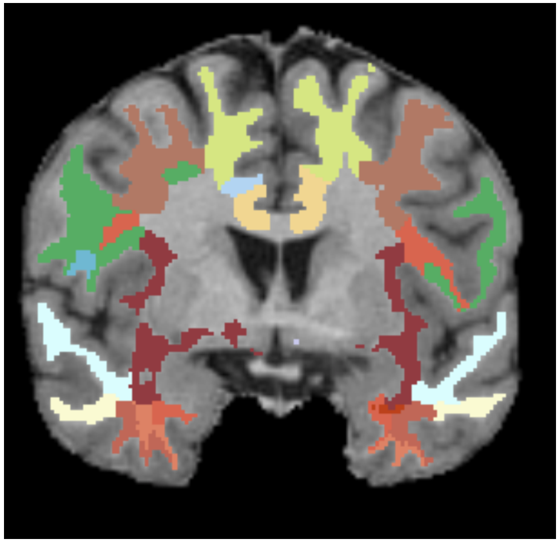
Results of quality control steps



Diffusion Data: Completed Work







Diffusion Data: Future Work

- Design processing pipeline for fiber tracking analysis
  - DWI/DTI atlas building with population (dwiAtlas, UNC)
  - Incorporation of multiple tensor data
  - Fiber tracking on atlas
  - Propagation of fibers to individual subjects
  - Examine scalar values along tracts in individual subjects
- Apply/extend full processing pipeline to full PREDICT-HD data set
- Design longitudinal statistical analyses

Methods: Aim 2.

- Construct an HD-specific
- Create tools for longitudinal analysis of changes in fiber tractography
- Perform whole brain longitudinal analysis of DTI connectivity using stochastic tractography tools for network and pathology detection.

Timeline: Year 2

- Aim1: Improve shape analysis tools and apply to larger cohort with multiple study visits
- Aim2: Longitudinal analysis of fiber tracts
- Aim3: Incorporate aim one and two workflows into XNAT instance