

# The National Consortium on Alcohol and Neurodevelopment in Adolescence (NCANDA): A Framework Supporting Neuroimaging Data Integration and Analysis



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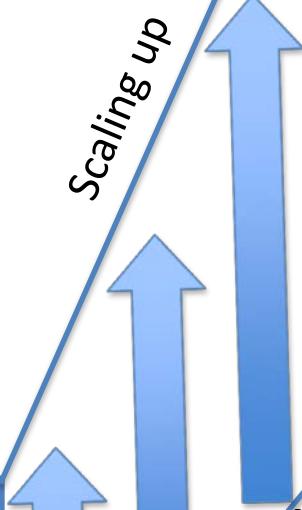
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National  
Consortium



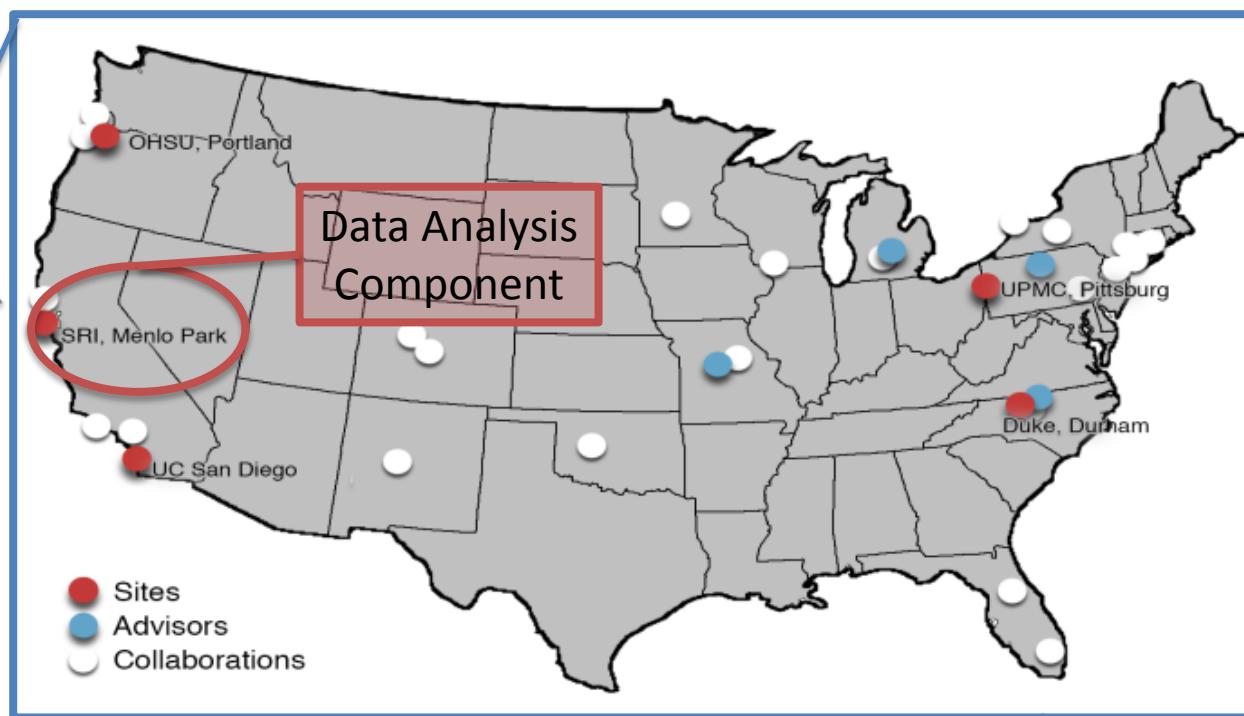
Traditional  
Research Lab



Longitudinal

Multi-Modal

# The Challenge



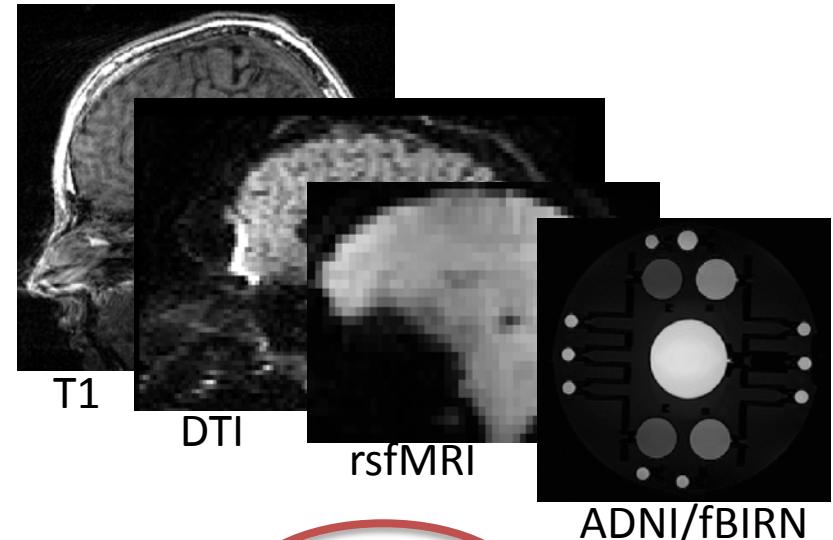
- Multi-Site
- Five sites across the US
  - Total of 808 enrolled participants
  - Baseline, 1 year, and 2 year follow-ups
  - Data collection initiated in 6 months
  - Limited resources for development
  - What are the system requirements?

# Requirements

## Clinical and Neuropsychological Instruments



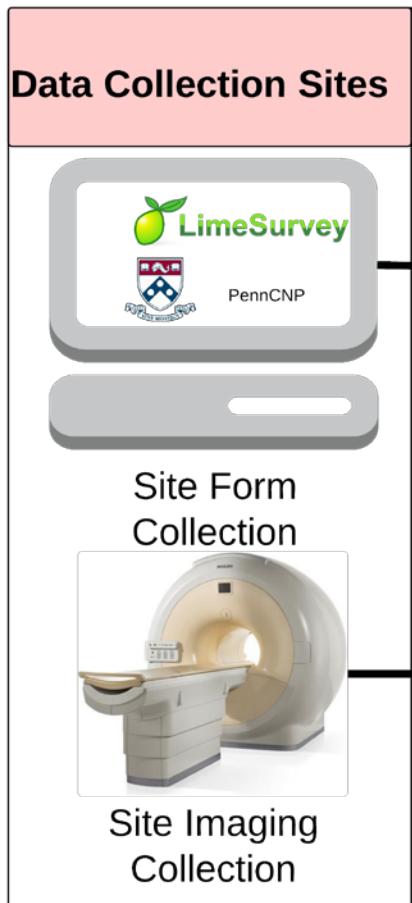
## Multimodal Imaging and Phantoms



- Accommodate heterogeneous instruments
- Validate data capture protocols
- Maintain ongoing data quality
- Ensure longitudinal visit time windows
- Automate as much as possible
- What Neuroinformatics resources to reuse, circa 2012?



# Overview and Approach



## Sites collect:

- Demographic Information
- Clinical Data
- Neuropsychological Test Scores
- MRI
  - Anatomical
  - Diffusion
  - Functional

# Clinical and Neuropsych Assessments

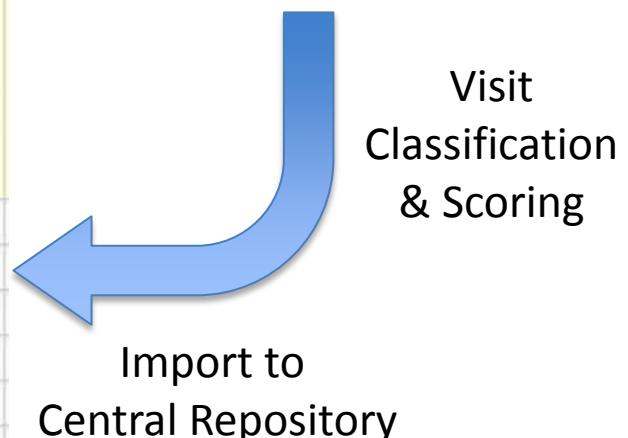


Record ID	Visit Information	Delayed Discounting, \$1000	Delayed Discounting, \$100	Paced Auditory Serial Addition Test (PASAT)
[REDACTED]	2013-03-13	●	●	●
[REDACTED]	2013-02-07	●	●	●
[REDACTED]	2013-02-26	●	●	●
[REDACTED]	2013-02-18	●	●	●
[REDACTED]	2013-02-21	●	●	●
[REDACTED]	2013-02-22	●	●	●
[REDACTED]	2013-04-01	●	●	●
[REDACTED]	2013-03-15	●	●	●
[REDACTED]	2013-03-18	●	●	●
[REDACTED]	2013-07-02	●	●	●

Cross-sectional REDCap Project

Subject ID	Basic Demographics Baseline visit (Arm 1: Standard Protocol)	Visit Date and Notes Baseline visit (Arm 1: Standard Protocol)	Visit Date and Notes 6-month follow-up (Arm 1: Standard Protocol)	Visit Date and Notes 1y visit (Arm 1: Standard Protocol)	Delayed Discounting, \$1000 Baseline visit (Arm 1: Standard Protocol)	Delayed Discounting, \$1000 1y visit (Arm 1: Standard Protocol)	Delayed Discounting, \$100 Baseline visit (Arm 1: Standard Protocol)	Delayed Discounting, \$100 1y visit (Arm 1: Standard Protocol)
[REDACTED]	●	●	●	●	●	●	●	●
[REDACTED]	●	●	●	●	●	●	●	●
[REDACTED]	●	●	●	●	●	●	●	●
[REDACTED]	●	●	●	●	●	●	●	●
[REDACTED]	●	●	●	●	●	●	●	●
[REDACTED]	●	●	●	●	●	●	●	●

Longitudinal REDCap Project



# Multi-Modal Imaging

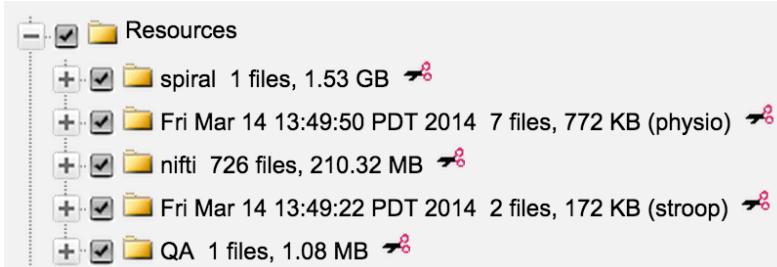


Sites Scans  
T1, T2, DTI, rsfMRI,  
ADNI/fBIRN Phantoms

Reading	
DateToDVD	2013-07-11
FindingsDate	2013-08-13
Findings	normal
QA Flags (TO BE SET ONLY BY QA STAFF)	

Scans			
Scan	Type	Series Desc	Usability
[+ 1]	ncanda-localizer-v1	ncanda-localizer-v1	unknown
[+ 2]	ncanda-calibration-v1	ncanda-calibration-v1	unknown
[+ 3]	ncanda-t1spgr-v1	ncanda-t1spgr-v1	usable
[+ 4]	ncanda-t2fse-v1	ncanda-t2fse-v1	usable
[+ 6]	ncanda-dti6b500pepolar-v1	ncanda-dtib500pepolar-v1	usable
[+ 7]	ncanda-dti60b1000-v1	ncanda-dtib1000-v1	usable
[+ 8]	ncanda-grefieldmap-v1	ncanda-grefieldmap-v1	usable
[+ 9]	ncanda-rsfmri-v1	ncanda-rsfmri-v1	usable

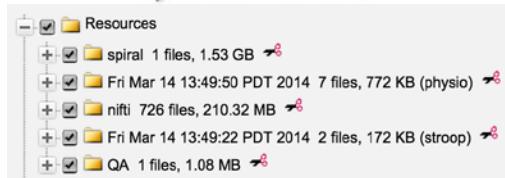
T1w MRI Scan Date	2015-05-28	Today	Y-M-D
Date of T1w image acquisition			
Age at T1w MRI Scan	21.9416167911	Age at T1w image acquisition	
* must provide value			
DTI Scan Date	2015-05-28	Today	Y-M-D
Date of DTI image acquisition			
Age at DTI MRI Scan	21.9416167911	Age at DTI image acquisition	
* must provide value			
Rs-fMRI Scan Date	2015-05-28	Today	Y-M-D
Date of rs-fMRI image acquisition			
Age at rs-fMRI Scan	21.9416167911	Age at rs-fMRI image acquisition	
* must provide value			



NIIfTI  
Conversion

- Semi-automatic QA
- Neuroradiologist readings
- Hourly/nightly QA reports
- Event-based workflow to populate image processing pipeline

# Data Analysis

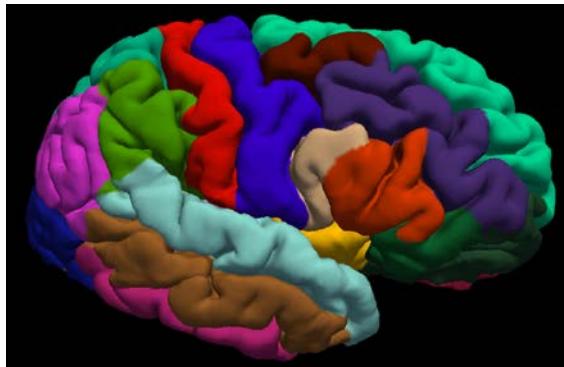


Import to  
Pipeline

Light Weight Data  
Pipeline

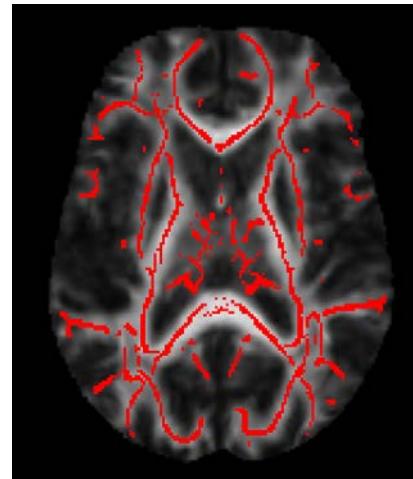
<http://www.nitrc.org/projects/lwdp>

Anatomical



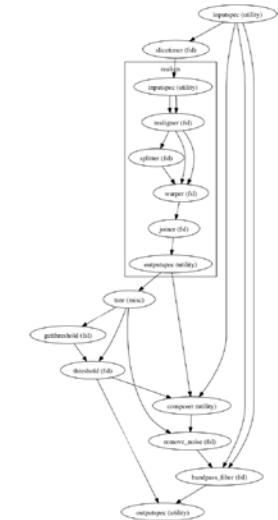
FreeSurfer Parcellation  
and Segmentation

Diffusion



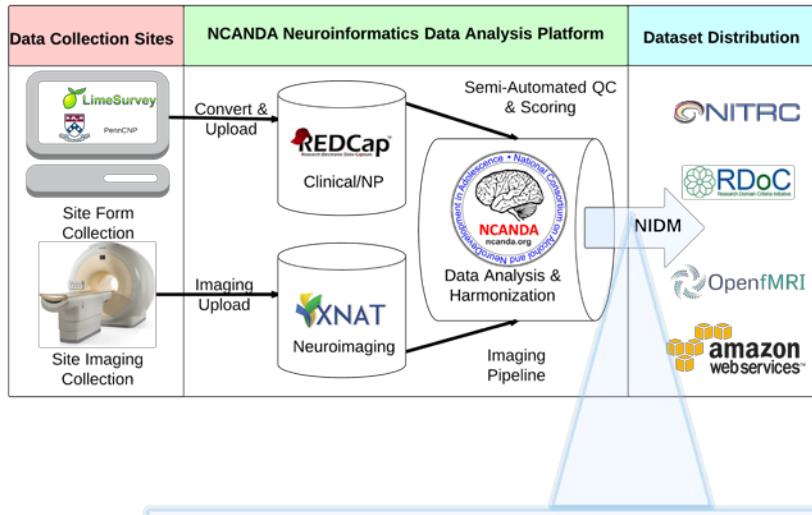
FSL Tract-Based  
Spatial Statistics

Resting State

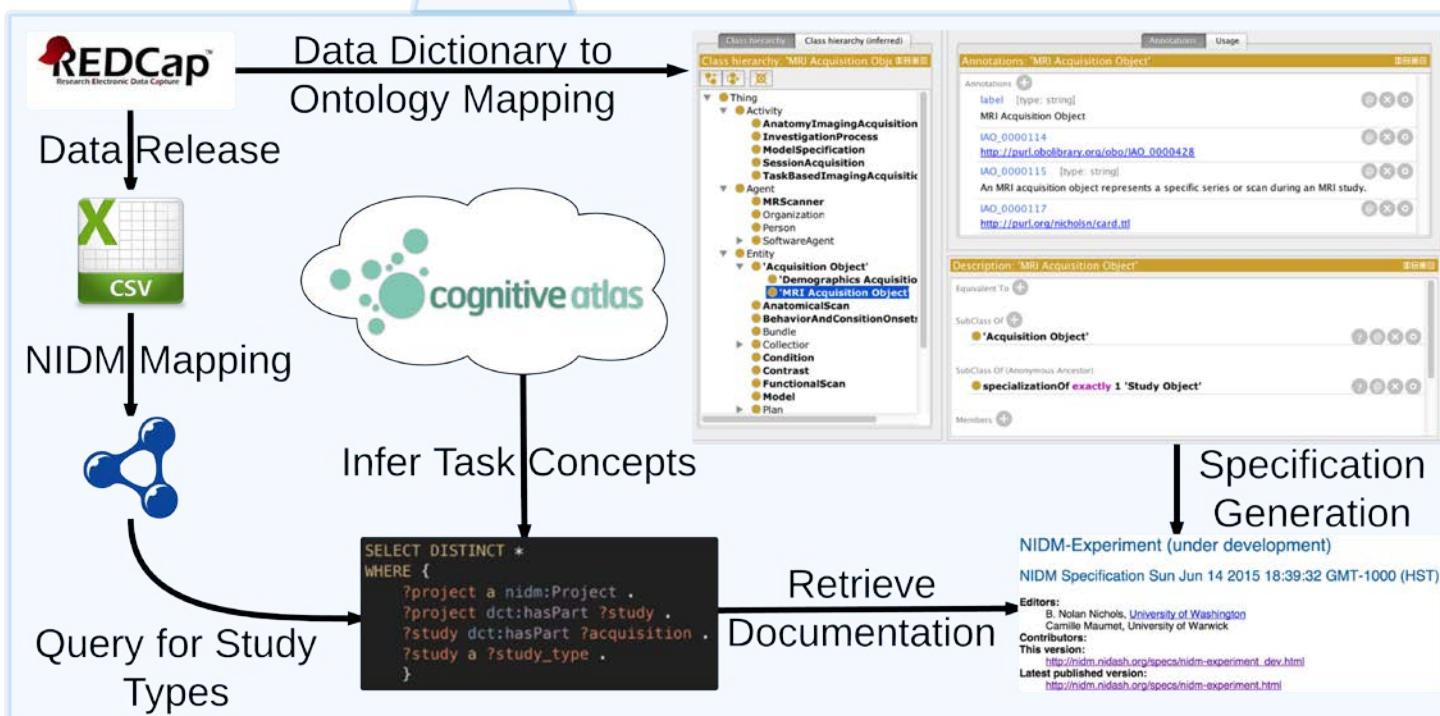


Nipype-based Preprocessing

# Next Steps and Data Sharing

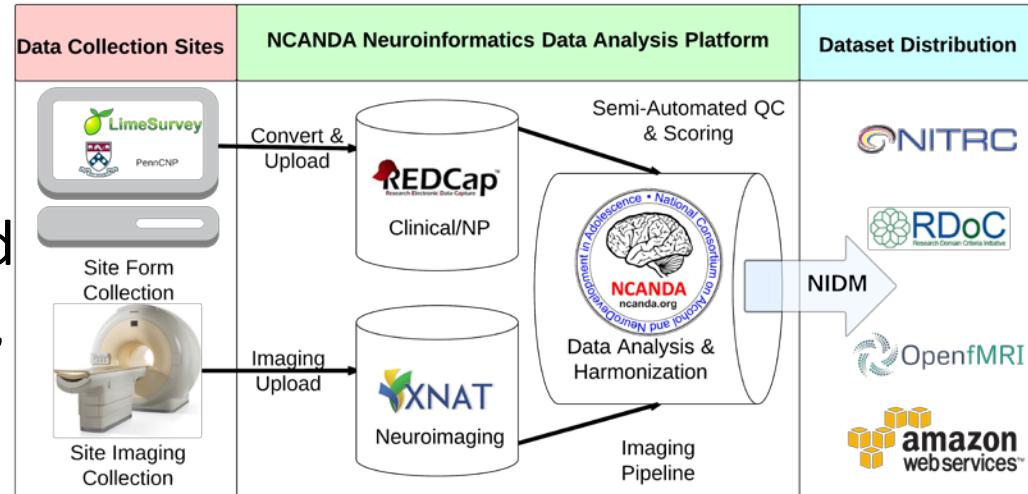


- Curated with REDCap data dictionaries
- Use Case for NIDM and BIDS Standards
- Adopt the NIDM process to curate data
- Develop object models of clinical, neuropsych, and imaging measures
- Demonstrate usage of NIDM for distributing NCANDA datasets



# Conclusions and Lessons Learned

- The ecosystem of Neuroinformatics software for imaging studies is mature
- Neuroinformatics tools can be reused and extended to develop scalable Neuroinformatics platforms
- Early involvement of informaticians may be able to simplify system architecture using common platforms
- Version Control Systems are an innovative way to capture data asynchronously before a data management system implementation
- Demonstrated the reuse of neuroinformatics tools to provide data integration and analysis hub for a multi-site, longitudinal study on adolescent development



<https://www.nitrc.org/projects/ncanda-datacore>

# Acknowledgements

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## Data Analysis Component

Weiwei Chu  
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Kilian Pohl  
\*Torsten Rohlfing  
Yong Zhang



## Data Sharing Task Force

Satra Ghosh  
Chris Gorgolewski  
David Keator  
JB Poline  
Jessica Turner  
... and many others!

# Neuropsychology Protocol

8 RFA-required functional domains; valid across wide age range

## *Executive Function & Attention*

Penn Continuous Performance Task  
LeJuez Distress Tolerance: PASAT  
SRI Stroop Match-to-Sample  
Penn Conditional Exclusion Task  
Penn Fractal N-back Task

## *Memory: Immediate-Delayed*

Penn Visual Object Learning  
Penn Word Memory  
Penn Facial Memory

## *Emotion Processing/Regulation*

Penn Emotion Recognition Task  
Penn Emotion Differentiation Test

## *Reward Seeking & Learning*

Stanger Delay Discounting Task

## *Visual Discrimination*

Landolt C - Acuity  
Ishihara – Color

## *Handedness & Dexterity*

Edinburgh Handedness Inventory  
Grooved Pegboard  
Penn Motor Praxis Task

## *Achievement*

Penn Vocabulary Test  
WRAT-4 Arithmetic

## *Intelligence*

Penn Logical Reasoning test  
Penn Matrix Analysis Test  
WRAT-4 Vocabulary

## *Classic Tests*

Rey-Osterrieth Complex Figure  
Ataxia – Walk-a-Line  
Digit Symbol Substitution

# Neuropsychology Test Battery

25 tests → ~250 primary variables from ~1000 measures

Test		
Ishihara Test		
Landolt C		
Edinburgh Handedness Questionnaire		May be completed during clinical assessment.
WRAT- 4 Reading		
<b>Penn WebCNP</b>		
Motor Praxis Test		
Penn Facial Memory Test		
Penn Word Memory Test		
Penn Continuous Performance Test-Number Letter Version		Administered on the MacBook Air. Must be completed in one session.
Short Fractal N- Back Test - 2 Back Version		
Penn Matrix Analysis Test		
Penn Facial Memory Test - Delayed		
Penn Word Memory Test - Delayed		
<b>Break</b>		
Penn Short Visual Object Learning Test		
Emotion Recognition Test		
Penn Conditional Exclusion Task		
Measured Emotion Differentiation		Administered on the MacBook Air. Must be completed in one session.
Penn Vocabulary Test		
Penn Logical Reasoning		
Short Visual Object Learning Test - Delayed		
Stroop Match to Sample		
Stanger Delay Discounting Task		Administered on the Dell laptop.
PASAT-C Lejeuz Distress Tolerance		
Rey-O Copy		
Rey-O Immediate		
WRAT- 4 Arithmetic		Must be completed in ~30 minutes.
Ataxia		
Grooved Pegboard		
Rey-O Delayed		
WAIS-IV Coding [Symbols can be distractors to the Rey-O]		

20 min.

5 min.

WebCNP  
60 min.

60 min.

Baseline NP battery = 180 min.  
Follow-up = 150 min.

# References

1. L. D. Johnston, P. M. O'Malley, R. A. Miech, J. G. Bachman, and J. E. Schulenberg, "Monitoring the Future national survey results on drug use: 1975-2014: Overview, key findings on adolescent drug use." 2015.
2. T. Rohlfing, K. Cummins, T. Henthorn, W. Chu, and B. N. Nichols, "N-CANDA data integration: anatomy of an asynchronous infrastructure for multi-site, multi-instrument longitudinal data capture," *Journal of the American Medical Informatics Association*, pp. amiajnl-2013-002367, 2013.
3. WebCNP: <https://webcnp.med.upenn.edu/>
4. LimeSurvey: <http://www.limesurvey.org/>
5. Blaise: <http://www.blaise.com>
6. ePrime: <http://www.pstnet.com/eprime.cfm>
7. Marcus, D., Olsen, T., Ramaratnam, M., & Buckner, R. (2007). The extensible neuroimaging archive toolkit. *Neuroinformatics*, 5(1), 11–33.
8. Subversion: <https://subversion.apache.org/>
9. Keator, D. B., Helmer, K., Steffener, J., Turner, J. A., Van Erp, T. G., Gadde, S., et al. (2013). Towards structured sharing of raw and derived neuroimaging data across existing resources. *NeuroImage*, 82, 647–661.  
<http://doi.org/10.1016/j.neuroimage.2013.05.094>