# ABCD STUDY: STUDY DESIGN, DATA SHARING & DEAP

Wesley K. Thompson | August 20, 2019

# **STUDY DESIGN**

- The complete collection of baseline data was released on the NIMH Data Archive (NDA) in March 2019.
- Baseline data are assessed on 11,878 subjects at 21 sites around the country.
- There are also follow-up assessments on a minority of these subjects.

# ABCD data dictionary (release 2.0)

# 27,400 x 65,000

## ABCD STUDY DESIGN (SHARED DATA IN 2.0)



## ABCD STUDY DESIGN – DATA RELEASE SCHEDULE

Release Year	Baseline	6 month	1 year	18 month	2 year	36 month	3 year	48 month	4 year	60 month	5 year	72 month	6 year	84 month	7 year	96 month	8 year	108 month	9 year	120 month	10 year	132 month	11 year	144 month	12 year
1	4,951	0																							
2	11,873	8,623	4,951	1,919																					
3	11,873	11,873	11,873	8,905	5,937	2,968	0																		
4	11,873	11,873	11,873	11,873	11,873	8,905	5,937	2,968	0																
5	11,873	11,873	11,873	11,873	11,873	11,873	11,873	8,905	5,937	2,968	0														
	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	8,905	5,937	2,968	0												
7	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	8,905	5,937	2,968	0										
8	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	8,905	5,937	2,968	0								
9	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	8,905	5,937	2,968	0						
10	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	8,905	5,937	2,968	0				
11	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	8,905	5,937	2,968	0		
12	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	8,905	5,937	2,968	0
13	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	8,905	5,937
14	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873	11,873
Collection year	0	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5	5.5	6	6.5	7	7.5	8	8.5	9	9.5	10	10.5	11	11.5	12

Yearly (rolling) release schedule

Baseline	Year 2	Year 4	Year 6	Year 8	Year 10
Year 1	Year 3	Year 5	Year 7	Year 9	Spreadsheet data (year 12) 21 visits, 11,873 participants, 65,000 measures = 16·10° values (16Billion) = 24GB

## **ABCD STUDY DESIGN**

# NESTED STUDY DESIGN IN ABCD

Dependencies between groups of participants violate the independence assumption. Any analysis should therefore account for the known dependencies before estimating unknown variables of interest.



# Missing data

✓ I don't know

- ✓ I don't want to tell you
- ✓ Truly missing
  - ✓ Messed up, never asked
  - ✓ Lost in transmission
  - $\checkmark$  We have answers but no participant ID
- Missingness by design (not missing)
  - ✓ By event type (e.g. no imaging data at non-imaging events)
  - ✓ New questionnaires/Variables are introduced missing before date
  - ✓ Missing because of branching logic

# DATA SHARING

## Shared data, opportunities/challenges

- ABCD Policy: All data is shared on an ongoing basis no holdout data. Any results published require a pre-release of that data.
  - Single channel for data release on National Data Archive.
- Share standard results such as results from QC pipelines and derived scores is good
  - lower barrier for analysis entry
  - use the community to provide feedback
  - promote best practices
  - reduce researchers degrees of freedom
- Requires additional resources for data curation, additional documentation, data sharing and communication towards the community. Exposes study to more challenging events.

# A study centric view of data harmonization

### Harmonization of no interest

Name changes require extensive coupling lists for quality assurance

### Harmonization of value

Coding of complex data during acquisition to allow for linkage to external information sources

## Supported now by NDA:

- Alias fields in data dictionary
- Study specific download packages

### Supported by ABCD:

- Use of RxNorm for medication inventory
- Use of consistent names for brain ROIs

# DEAP applications for specialized domains



#### Medications

Anatomical Therapeutic Chemical (ATC1-4)

NERVOUS SYSTEM

Not a drug

**RESPIRATORY SYSTEM** 

**PSYCHOANALEPTICS** 

PSYCHOSTIMULANTS, AGENTS USED FOR ADHD AND NOOTROPICS

Centrally acting sympathomimetics

ANTIHISTAMINES FOR SYSTEMIC USE

CARDIOVASCULAR SYSTEM

Vitamin

/ Ibuprofen 20 MG/ML Oral Suspension [Motrin	
	Э. <u>vdn 0.003</u>
Ibuprofen 100 MG	
ardunga entre andrugate for tai Ibuprofen 200 MG	Cream [El
Ibuprofen 100 MG/ML	
ur cardiac propa Ibuprofen 100 MG Chewable Tablet [Advil]	Net (Advil)
Ibuprofen Pill	1 Oral Su
Ibuprofen 400 MG	1
Ibuprofen 200 MG Oral Tablet	
Ibuprofen 50 MG	
Ibuprofen 800 MG	nexj ⊭∠ sd Release
Ibuprofen Oral Suspension	
Ibuprofen 20 MG/ML Oral Suspension [Motrin]	
er Nockers (AM) Ibuprofen Chewable Product	20 MG Or aar] #1
M - ACE inhibitors, plain #1O 1162653 Enale O 316151 Liking	ıpril Pill #1 sril 10 MG #1

DATA EXPLORATION AND ANALYSIS PORTAL (DEAP)

# Data Exploration and Analysis Portal

Web-based interface, cloud deployment NIMH's NDA data sharing platform as data source Access to all ABCD measures shared in NDA17 Build-in nesting for multi-level covariates of choice Access to visualizations and statistical model summary

## Shared ABCD data

Available on National Data Archive (nda.nih.gov) requires signup and support from institution

11,875 participants data available since early 2019 3.2GB spreadsheet data (\*.tsv) 23TB MRI (300Gb T1/T2)

65,000 measures per participant (>67% from imaging)

Resources: Source code repositories - github.com/ABCD-STUDY/ Data Analysis and Exploration Portal

# ABCD open science [1 Team, 15 members, 33 git repositories]

enroll Participant enrollment system hosting sensitive data	Ar	edcap-to-nda xporting REDCap data dictionaries and data to the NIMH National Data rchive (NDA) JavaScript	M.M
Data Exploration and Analysis Portal of the ABCD Study ● JavaScript ★ 2	a	uto-scoring isual programming to calculate derived scores for REDCap	~^~~
Collection of scripts to analyze ABCD release data nda17 abcd-study ★ 6 % 5 Updated 2 days ago	e	Python Updated on Jun 25	۸
redcap_rewrite_history         Change the name of REDCap items in an existing project and attempt to rewrite the projects history.         ● PHP ★1 ④ GPL-3.0 Updated 5 days ago	A	ABCDWorkshop-reproducible-science Material collection for the ABCD-DAIC workshops on data science JavaScript Updated on Jun 16	
FIONASITE         Data upload site for FIONA site computer         JavaScript       §1         Updated 7 days ago         complete_row	ti c	imeline-followback Online timeline-followback subject test JavaScript Updated on Apr 24	
REDCap extension module: Colors each row of an instrument - if a value has been provided. This will highlight rows with missing values to improve their visibility. PHP	^ I	nih-ipad-app-end-point An end-point for centrally storing data from the NIH iPad app ● PHP   ♀1   Updated on Apr 20	
CIFTI-Analysis Scripts to enable vertex-wise (CIFTI) analysis of ABCD with FSL/PALM and HCP Workbench		geocoding A framework for adding gelocation derived data to the ABCD study. ● R 회 MIT Updated on Apr 4	

Python ★1 Updated on Aug 16

#### FIONA-QC-PHANTOM

Online QC operations performed on Phantom MRI data

Matlab ★1 ¥1 Updated on Mar 23

#### Fast-Track-Image-Sharing

The ABCD study shares data on the National Data Archive. This project provides the tools for sharing.

nda dicom-images anonymization

Python 1 Updated on Feb 7

#### Minimally-Processed-Image-Sharing

Python ★ 2 Updated on Dec 5, 2017

#### little-man-task

The little man task web-based instrument

JavaScript Updated on Nov 30, 2017

#### redcap-completion

Measure item level completion in a large REDCap project

JavaScript Updated on Nov 11, 2017

#### simple-t1-motion-detection

Measures the amount of ghosting artifacts in T1-weighted images

C++ Updated on Jul 27, 2017

#### tick-tock

Study Observation system monitoring events per day

JavaScript Updated on Jun 23, 2017

#### numerical-fitting

Client side numerical computation library written in javascript.

JavaScript Updated on Dec 28, 2016

#### aux-file-upload

PHP Updated on Dec 2, 2016

#### **FIONA-protocol-compliance**

Matlab script for ABCD study protocol compliance

Matlab Updated on Nov 28, 2016

#### redcap-hook-framework

Forked from 123andy/redcap-hook-framework

The REDCap hook framework is a means to organize and deploy custom hooks in a single project or across the entire instance.

● PHP ★ 1 😵 16 Updated on Nov 4, 2016

#### **ABCDreport**

PHP Updated on Sep 6, 2016

#### pearson-central-end-point

An end-point for centrally storing data from the Pearson's Q-interactive.

PHP Updated on Jun 7, 2016

#### delay-discounting

Delay-discounting task measuring impulsivity

JavaScript Updated on Aug 11, 2016

USERNAME: ADMIN

001100111011100

011100100110010101

ABCD

Adolescent Brain Cognitive Development Data Exploration and Analysis Portal

GETTING STARTED OO PLAN O1 Explore O2 Limit O3 Analyse O4 Extend

# **DEAP SCIENCE** Data Exploration and Analysis Portal

A service provided by the Data Analysis and Informatics Center of the ABCD study

#### ABCD Ontology Viewer Home



#### interview\_age

examples: intelligence, schizophrenia, ADHD

More than 101 results (0.11 seconds)

## interview\_age in ABCD Children's Report of Parental Behavioral Inventory / crpbi01 [Parenting]



search term: interview\_age - matches element name

Age in months at the time of the interview/test/sampling/imaging.

Age is rounded to chronological month. If the research participant is 15-days-old at time of interview, the appropriate value would be 0 months. If the participant is 16-days-old, the value would be 1 month.

interview\_age in ABCD Cash Choice Task / cct01 [Task Based] search term: interview\_age - matches element name

## Explore 44,000 ABCD measures

?

#### Females only Result of the current restriction Nay: 2,372 Yea: 2,152 key: #9172 .

Visual sub-setting data exploration

#### [admin] bmi\_calc\_example The body mass index calculated from the height and weight va... close Element Name (user admin - public score) bmi calc example anthroheightcalc anthroweightcalc eventname 1,300 = 1,200 -18.234 56.5 82.8 bmi\_calc\_example baseline\_year 1,100 20.15 56.5 91.5 baseline\_year 1,000 900 -Axis label 15.174 baseline\_year 57.3 70.8666666666667 800 -700 -The body mass index calculated from the height and weigh 19.993 53.5 81.4 baseline\_year 600 -500 -17.663 58.3 85.4 baseline\_year 400 -Save as private 300 -Save baseline\_year 16.213 54.5 68.5 200 -20.468 55.35 89.2 baseline\_year 100 -0. 34.171 63.5 196 baseline vear 0 5 10 15 20 25 30 35 40 45

### The Body-Mass Index (BMI)

The body-mass-index (BMI) depends on the height and weight of the participant. These two values exist for each participant in DEAP. We need to copy these values by calling the use-function into our browser window. As a return value use returns a list of promises that are fulfilled once all the data arrives.

```
var promises = use(["anthroweightcalc", "anthroheightcalc"]);
```

The BMI can be calculated using the following formula - assuming pounds as units for weight (*w*) and inches as units for height (*h*):

We can implement this calculation in a function called calc that gets two arguments, the weight of a participant in w and the height of a participant in h. The function then returns the calculated values.

```
function calc(w, h) {
     return w/(h*h) * 703;
```

Now we wait until the promises have been resolved, which indicates that the weight and height values are available. At this point we can get the data and compute the new variable anthro\_weight\_calc using map. The map function computes for each row of the data spreadsheet the value of the new variable. It is sufficient to row.set the new value to have it show up in the histogram and table of this variable:

```
Promise.all(promises).then(function() {
    ven data - nev DataErama(allMaacurac)
```

Autosaved: 2:30 pm lines: 27 words: 297 0:0 2 Keystrokes

## Notebook style, user defined derived measures

$$703\frac{w}{h^2}$$

$$03\frac{w}{h^2}$$

# Multilevel Data Analysis

Multilevel statistical models for baseline data reflect the multilevel study design (GAMM4).

$$Y_{sfi} = \beta_0 + x_{sfi}\beta + z_{sfi}\gamma + a_s + b_{f(s)} + \epsilon_{sfi}$$

- x<sub>sfi</sub> are covariates (e.g., demographics)
- z<sub>sfi</sub> are independent variables of interest
- a<sub>s</sub> is a site-specific random effect
- b<sub>f(s)</sub> is a family random effect nested within site

This model is extendable to non-normal outcomes (e.g., discrete, count variables).

## **ABCD STUDY DESIGN**

- Of these 11,875 subjects, family units include:
  - 8,150 singletons
  - 1,600 non-twin siblings
  - 2,100 twins (1,050 pairs)
  - 30 triplets (10 sets)

## **ABCD STUDY DESIGN**



# **Tutorial Mode on DEAP**

Not familiar with generalized additive mixed models for the analysis of longitudinal data in a multi-site project with a complex family structure? Deap provides a training-wheel mode with in-depth explanations on how to interpret your model.

an independent variable again. Use the buttons to toggle off the inclusion of any of the fixed effect covariates. Both site and family are always included into the model as random effects as they are part of the study design.



## Data Display and Summaries

Fig. 2: Data distributions for dependent (left) and independent variable (right).

Histograms are used to inspect the distributions of the data used in the model. For the dependent variable (Fig. 2, left) we want to make sure that they are roughly normally distributed (bell-shaped). In particular we want to check if there are outliers or, if the distribution is highly skewed. If large

In particular we want to check it there are outhers of, it the distribution is inghty skewed. It take

## Hypothesis Testing on DEAP

Can changes in anxiety be explained by cognitive development scores measured in the picture vocabulary test, if one corrects for known covariates?

### A Model specification

ndependent Variable cbcl_scr_syn_anxdep_t									
Dependent Variable nihtbx_picvocab_uncorrected									
User Covariates								Submit	
Fixed Effect Covariates	Race/Ethnicity	GENDER	EDU	INC	MARITAL	AGE			
Random Effects	SITE FAMILY								

### C Regression model fit



### B Data used in the model



## D Result tables / Model comparisons

	Estimate	Std. Error	t value	Pr(>   t  )	sig
(Intercept)	52.27064	1.77974	29.37	< 1e-6	•••
nihtbx_picvocab_uncorrected	0.02316	0.01322	1.75	0.0798201	
race.ethnicityBlack	-1.15741	0.37474	-3.09	0.0020246	**
race.ethnicityHispanic	-0.14640	0.30244	-0.48	0.628372	
race.ethnicityAsian	-1.21511	0.66369	-1.83	0.0671952	
race.ethnicityOther	0.13576	0.33444	0.41	0.6848096	
genderM	0.67781	0.18458	3.67	0.0002436	• • •
high.educBachelor	-0.05391	0.54923	-0.10	0.9218111	
high.educHS Diploma/GED	-0.90738	0.57636	-1.57	0.1154924	
high.educPost Graduate Degree	-0.17039	0.56453	-0.30	0.7628061	
high.educSome College	-0.06243	0.52201	-0.12	0.9048016	
marriedyes	-0.40629	0.24155	-1.68	0.0926505	
interview_age	-0.00946	0.01301	-0.73	0.4672105	
household.income[< 50K]	1.12847	0.32764	3.44	0.0005784	***
household.income[> =50K& < 100K]	0.48843	0.24194	2.02	0.0435734	*

## Feature: Expert Mode

Access to the (R) source code behind the GAMM4 model. Can be edited by the user and becomes part of a sharable resource for download and to other DEAP users.

GAMM4 Home Tutorial

This application fits generalized additive mixed models using the R package GAMM4 (Simon Wood, Fabian Scheipl). The GAMM model is appropriate for both cross-sectional and longitudinal regression analyses and allows for an explicit modelling of aspects of the study design such as nesting of subjects within sites data collection and family structures such as twin pairs and other siblings.

Dependent Va	riable (	Y-axis)						
nihtbx_fluidcomp_uncorrected								
Independent \	/ariable	(X-axis	s, for p	plotting)				
dti_fiber_fa_	l_ifo							
Grouping Varia	able (fo	r intera	ction a	and plotti	ng)			
Fixed Effect C	ovariate	es	INC		405			
Race/Ethnicity	SEX	EDU	INC	MARITAL	AGE	J		
	ts							
Expert Mode (	testing	and de	ebuggi	ng)				



## **DEAP Updates**

- Docker deployment of DEAP (github.com/ABCD-STUDY/DEAP).
- Pre-registration workflow supporting model specification with variable selection and appropriate variable transformations. Text is provided for sampling, design, and analysis plan as well as for the analysis scripts.
- Subset analysis of participants.
- User defined derived variables with data dictionary entries and scoring algorithms (sharable).
- Upcoming:
- Allow for
  - additional projects shared on DEAP (NDA17, NDA18),
  - additional participants (add to our replace ABCD cohort)

#### Dependent Variable (Y-axis)

nihtbx\_fluidcomp\_uncorrected

#### Independent Variable (X-axis, for plotting)

nihtbx\_picvocab\_uncorrected

#### Grouping Variable (for interaction and plotting)

#### Select subset of sessions

Other Independent Variables



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#### **Fixed Effect Covariates**

Race/Ethnicity SEX EDU Income Marital AGE

Random Effects

FAMILY SITE

Expert Mode (testing and debugging)



Analyze

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This application fits generalized additive mixed models using the R package GAMM4 (Simon Wood, Fabian Scheipl). The GAMM model is appropriate for both cross-sectional and longitudinal regression analyses and allows for an explicit modelling of aspects of the study design such as nesting of subjects within sites and family, twin pairs and other siblings.

Dependent Variable (Y-axis)		
nihtbx_fluidcomp_uncorrected	+	လ
Independent Variable (X-axis, for plotting)		ndu
nihtbx_picvocab_uncorrected	+	≓÷
Grouping Variable (for interaction and plotting)		
•		
Select subset of sessions		
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Other Independent Variables		
	+	
Fixed Effect Covariates		
Race/Ethnicity         SEX         EDU         Income         Marital         AGE		
Random Effects		
FAMILY SITE		
Expert Mode (testing and debugging)		
Fig. 1: Model specification used to define and execute the stat	istical model.	

#### 10.17sec for calculation

The model specified in Fig. 1 is used to estimate the statistical relationship between an independent variable and a measured dependent variable. In the generated model plot (Fig. 3) the independent variable is displayed on the X-axis and the dependent variable appears on the Y-axis. Both measures are user defined and can be selected from a list of available measures. Whereas the independent variable can be of any type (categorical or continuous), and there are no

## Analysis tutorial mode – expert commentary

```
Model Builder Deap Model Builder Debug
```



## Advanced Usage (Model Builder)

A collaborative environment to integrate advanced statistical analysis features into ABCD. The model builder is software agnostic. R modules coexist next to python/pandas, Matlab. Data frames are used for inter-nodal communication. System provides computational cloud resources and each block can be extracted from the system (data and source-code) for documentation and offline analysis.



## Data flow graph (graphical programming) of the Model Builder on DEAP

## ACKNOWLEDGEMENTS

- The NIMH Data Archive (NDA)
  - Greg Farber
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  - Fangzhou Hu
  - Chase Reuter
- ABCD Biostatistics Work Group