

Vermont Center on Behavior and Health



HEALthy Brain and Child Development Babies · Brains · Bright Futures

Insights about Substance use from Development Neuroimaging Studies: an Update on the ABCD and HBCD Studies

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Todays Talk

- The ABCD Study
 - Overview
 - Update
 - A few results
- The HBCD Study
 - Overview
 - Update
- Questions

ADOLESCENCE IS A TIME OF DRAMATIC CHANGES IN BRAIN STRUCTURE AND FUNCTION.





Nora Volkow, Ph.D.; Director National Institute on Drug Abuse

A large longitudinal study beginning in early adolescence will help us understand the <u>normal variability</u> in brain and cognitive development and <u>tease apart the many factors that influence it</u>.

"Thus, the Adolescent Brain Cognitive Development study was created to answer the most pressing public health questions of our day."

www.ABCDstudy.org

- 10-year longitudinal study of 11,878 children (2,100 twins) enrolled at ages 9-10; 21 data collection sites in the United States
- Administrative and Data cores at UCSD
- Recruitment through schools epidemiologically informed, once a school was selected, all students who were age 9-10 were invited to participate
- Twins recruited through birth registry at twin-sites





Adolescent Brain Cognitive Development ™ Teen Brains. Today's Science. Brighter Future.

- Goal was to recruit a sample that broadly reflected the US population of 9–10-year-olds (in 2015) based on data from the American Community Survey.
- Baseline 11,878 families recruited in 24 months (575 families in Vermont)





ABCD Initiated by NIH Collaborative Research on Addiction (CRAN)

- NIDA, NIAAA, National Cancer Institute
- Many other federal collaborators are now participating

Federal Collaborators: Teen Brains. Today's Science. Brighter Future.

National Institute on Drug Abuse	National Institute on Alcohol Abuse and Alcoholism		National Cancer Institute	National Institute of Mental Health
NIH Office of Behavioral and Social Sciences Research	<i>Eunice Kennedy</i> <i>Shriver</i> National Institute of Child Health and Human Development	National Institute of Neurological Disorders and Stroke	National Institute on Minority Health and Health Disparities	NIH Office of Research on Women's Health
National Science Foundation	Centers for Disease Control and Prevention - Division of Violence Prevention	Centers for Disease Control and Prevention - Division of Adolescent and School Health	National Institute of Justice	National Endowment for the Arts

ABCD Youth Protocol Summary: Baseline

Neurocognition

Picture Vocabulary

• Flanker Inhibitory Control &

List Sorting Working Memory

• Dimensional Change Card Sort

Pattern Comparison Processing

Picture Sequence Memory

Oral Reading Recognition

NIH Toolbox Tasks:

Attention

Speed

Physical Health

PhenX Anthropometrics (height/ weight/waist measurements) Snellen Vision Screener Edinburgh Handedness Inventory Youth Risk Behavior Survey: Exercise Pubertal Development Scale Menstrual Cycle Survey (pubescent girls)

Brain Imaging

Screen Time Survey

Structural MRI

- 3D T1 Weighted
- 3D T2 Weighted
- Diffusion Tensor Imaging
- Functional MRI (fMRI)
- Resting StateMonetary Incentive Delay Task
- Stop Signal Task
- Stop Signal lask
- Emotional N-Back Task

Biospecimens

Breathalyzer and Oral Fluids (subset) Saliva Samples for DNA, Puberty Blood Samples (subset)

Hair Sample Baby Teeth

Mental Health Kiddie Schedule for Affective Disorders and Schizophrenia

Background Items SurveyDiagnostic Interview for DSM-5

(5 modules) PhenX UPPS-P for Children Survey

PhenX Behavioral Inhibition/ Behavioral Approach System (BIS/BAS) Scales

Prodromal Psychosis Scale Youth Resilience Scale



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Culture & Environment

Prosocial Tendencies Survey PhenX Acculturation Survey

Parental Monitoring Survey

Acceptance Subscale from Children's Report of Parental Behavior Inventory (CRPBI) - Short

PhenX Family Environment Scale - Family Conflict PhenX Neighborhood Safety/

Crime Survey PhenX School Risk & Protective Factors Survey

Substance Use

For most participants*:

Timeline Follow-Back Survey PhenX Peer Group Deviance Survey PATH Intention to Use Tobacco

Survey Caffeine Intake Survey

ente intake Survey

Participant Last Use Survey (PLUS) for substance use within the last 24 hrs

Other Data Sources

Geocoding from Residential History School Records FitBit® (subset) Brief Problem Monitor -Teacher Form

*For participants with differing levels of substance use (low, moderate, heavy), follow-up items include: iSay II Q2 Sipping items; Tobacco Low-Level Use Measure; MJ Low-Level Use Measure; PhenX Acute Subjective Response to Alcohol, Tobacco, or MJ; Hangover Symptom Scale; Rutgers Alcohol Problem Index (RAPI); Nicotine Dependence (PATH); Drug Problem Index (MAPI); MJ Problem Index (MAPI)

Rey Auditory Verbal Learning Task Cash Choice Task Little Man Task Matrix Reasoning Task

RAVLT Delayed Recall

ABCD Open Science Model –

A Unique Resource for the Entire Scientific Community

Open sharing through the NIMH Data Access Portal (NDA).

- •Goal to allow scientists worldwide to conduct "Big Data" analyses, pool resources, and enrich the value of this study.
- •Anonymized raw neuroimaging data, within one month of data collection
- •Curated derived data, annually, beginning 1 year after start of data collection

Adolescent Brain Cognitive Development



UVM ABCD Cohort 2017 (age 9-10)



UVM ABCD Cohort 2019 (age 11 - 12)

ABCD STATUS UPDATE

- Currently collecting Year 6 Follow-up data (ages 15-16)
- 97.9% sample retention in the ABCD Study!
- Remote data collection during the pandemic.



But note that we have unknown numbers of *de facto* withdrawals and participants at risk for withdrawal.

Funded Grants Leveraging ABCD Data



N=73

Funded Grants Leveraging ABCD Data





Publications Using ABCD Data



Publications – Unexpected Focus Areas

Research Letter

May 17, 2021

Prevalence of Perceived Racism and **Discrimination Among US Children** Aged 10 and 11 Years

The Adolescent Brain Cognitive Development (ABCD) Study

PNAS

Adolescent civic engagement: Lessons from Black Lives Matter

PAIN



New research

Racial Disparities in Elementary School Disciplinary Actions: Findings From the **ABCD** Study

New Research

Association Between Discrimination Stress and Suicidality in Preadolescent Children



in children

Nucleus accumbens cytoarchitecture predicts weight gain in children

Polygenic Risk for Insomnia in Adolescents of Diverse Ancestry

nature communications

frontiers

in Genetics

Associations between frontal lobe structure, parentreported obstructive sleep disordered breathing and childhood behavior in the ABCD dataset

Paediatric Neuroradiology Published: 11 July 2021

Imaging and health metrics in incidental cerebellar tonsillar ectopia: findings from the Adolescent Brain Cognitive Development Study (ABCD)

differences in brain structure



Original Article 🔂 Full Access

Early adolescent gender diversity and mental health in the Adolescent Brain Cognitive Development study

PLOS ONE

Screen time and early adolescent mental health, academic, and social outcomes in 9- and 10- year old children: Utilizing the Adolescent Brain Cognitive Development [™] (ABCD) Study



Environment International Volume 143, October 2020, 105933

determinants of sex differences in the pre-Fine particulate matter exposure during adolescent brain childhood relates to hemispheric-specific

Ehsan Adeli ^{a, 1}, Qingyu Zhao ^{1, a}, Natalie M. Zahr ^{a, b}, Aimee Goldstone ^b, Adolf Pfefferbaum ^{a,} Edith V. Sullivan ^a, Kilian M. Pohl A^{a, b}

Deep learning identifies morphological

NeuroImage 223. December 2020, 11729





Early Adolescent Substance Use Before and During the COVID-19 Pandemic: A Longitudinal Survey in the ABCD Study Cohort

Some key findings from ABCD

- Small effect sizes and the need for large samples (Owens)
- Scientific Training in Addiction Research Techniques (START)
 - Family history of SUD related to brain cortical thickness trajectories (Dibbs-Goncalves)
 - Adolescent positive alcohol expectancies links to response inhibition and brain function (Adams)
- Effects of prenatal cannabis exposure on adolescent development (Cioffredi)



Article

Reproducible brain-wide association studies require thousands of individuals



Marek, et al. Nature 603.7902 (2022)



Resetting Expectations: Big Data and Small Effects

Owens et al., PLOS One, 2021

195 summary scores from ABCD baseline data yielding 6,669 correlations

- Sleep & total mental health problems (r=.58)
- ASR Parent total psychiatric problem & CBCL child total psychiatric problems (r=.57)
- Fluid intelligence & crystalized intelligence from NIH toolbox (r=.48)
- Age & height (r=.43)
- Parent report of how well child does in school & CBCL Attention problems (r=.43)
- Parent report child has received mental health services & CBCL total problems & (r=.40)
- Parent income and parent reported neighborhood safety (r=.36)
- # of traumatic experiences & CBCL total psychological problems (r=.20)
- Age & pubertal development (r=.17)
- UPPS lack of planning & CBCL attention problems (r=.17)
- Weight & screen time (r=.16)
- CBCL Internalizing symptoms & suicidality (r=.16)
- Parent report Family HX of mental health services & CBCL total problems (r=.15)
- Child report parental acceptance & CBCL total problems (r=.09)
- UPPS lack of planning & detention frequency parent report (r=.08)
- Sleep problems & total IQ (r=.06)
- Physical activity & weight (r=.03)

Resetting Expectations: Big Data and Small Effects



Also essentially unchanged if you add nuisance covariates or apply statistical thresholds and

[Owens et al., PLOS One.]





Why we need large cohort studies

- Improve reliability of reported associations.
- Intense phenotyping enable research across disciplines – comprehensive look at neurodevelopment.
- Robust analytic methods (i.e., built in replication)
- Disentangle confounded demographics
- Ability to analyze sub-groups matched on particular features to interrogate specific research questions.



SIAT

Frontal **cortical thickness trajectories** among 9–13-year-old preadolescents with a positive versus negative family history of alcohol/substance use problems.





Exposure:

- FH Positive (FHP) (24.8%, n=2,696): having ≥1 biological parents and/or ≥2 biological grandparents
- FH Negative (FHN) (61.4%, n=6,675), having no parents/grandparents with alcohol/substance use problems
- **Preadolescents with only 1 grandparent** with a history of substance problems (13.9%, n=1,507) were not included in our models.

- Cortical thickness changes in frontal regions (particularly pre- and paracentral regions) were significantly associated with FHP, with overall <u>more</u> <u>rapid thinning.</u>
- The population is largely substance naïve, supporting prior research showing neurological development of youths may be affected by parental history of alcohol/substance use problems.



Are positive alcohol expectancies related to response inhibition and brain function?

Alcohol expectancy: personal beliefs that a particular behavioral, emotional or cognitive effect will occur when drinking alcohol.

Positive expectancy is related to earlier alcohol initiation and subsequent use. It may have value as a modifiable factor that could be strategically leveraged for prevention efforts

Response inhibition: ability to stop a pre-potent response – measured with a cognitive task (the stop signal task).

Task performance is related to other forms of impulsivity including ADHD, and SUD. The stop task is one of the fMRI tasks in ABCD

Positive alcohol expectancy may be related to response inhibition – this may lead to a better understanding of the brain mechanisms by which our beliefs relate to health behaviors.

Alcohol helps a person relax, feel happy, feel less tense, and can keep a person's mind off of mistakes at school or work.	1;2;3;4;5
Alcohol can help how well a person gets along with others (makes people want to have fun together).	1;2;3;4;5
Alcohol helps people think better and helps coordination (people understand things better; can do things better).	1;2;3;4;5 (



Results: Positive AE was associated with lower activation in the right anterior insula during response inhibition.





Prenatal cannabis exposure (PCE)

- Cannabis use during pregnancy is increasing in prevalence, frequency, and quantity of use.
- THC readily crosses the placenta and accumulates in fetal tissue.
- The endogenous endocannabinoid system plays a critical role in early brain development.
- Long term effects of exposure remain unclear with the National Academies of Sciences, Engineering, and Medicine concluding in 2017 that only reduced birth weight was robustly linked to exposure.



NASEM 2017

Adjusted prevalence of past-month cannabis use



A case-control study of prenatal cannabis exposure (PCE)

- Prenatal cannabis exposure after knowledge of pregnancy (n=224).
- Tobacco/alcohol exposed group matched on age & sex (n=224).
- Non-exposed group matched on age & sex (n=224).
- Poisson mixed models (family nested within site).
- Covariates:
 - Factors related to childhood ADHD: parental psychopathology, maternal age, duration of breastfeeding.
 - Factors related to neurodevelopment: prematurity, birthweight.
 - Demographics not equivalent after matching: race/ethnicity, household education
- Outcomes included vertex-wide analysis of the 3 fMRI tasks.
- PCE associated with increased attention and externalizing problems (both parent and teacher report) and parent reported thought, and social problems.
- Notably no effects of cognition, or brain activation measures from the 3 fMRI tasks after covariates.

Attention



Marginal Means of CBCL symptoms







Ciofreddi et al 2022

Motivation for *another* large, longitudinal, developmentalneuroimaging study

- Challenges with retrospective report of prenatal environment
- Improved measures are critical for understanding the effects of the prenatal environment.
- Many things happen during early development hard to untangle prenatal from postnatal effects.
- The HEALthy Brain Child
 Development (HBCD) Study
 is designed to address

is designed to address some of these issues.

• Synergies between HBCD and ABCD are built in.





HEALthy Brain Child Development Study



- Prospective longitudinal study of child development from pregnancy through first 10 years of life
- Target sample size 7,500 mother child pairs recruited in mid-pregnancy over a ~3 year period of time
- 25 recruitment sites across the U.S. representing diversity of the population of pregnant persons giving birth.

Over-sampling of substance using pregnant people



- 25% overall target for any SU ≥12% opioid ≥ 12% marijuana ≥ 12% alcohol ≥ 12% tobacco
- Based on estimates of pregnancy substance use in NSDUH and polysubstance correlations
- □ Will require most enhancement for opioid use (~1% in NSDUH)
- Only modest enhancement for marijuana and alcohol (8% marijuana, 10% alcohol, in NSDUH).
- Tobacco use is prevalent in the general population of pregnant women (12% tobacco in NSDUH)

HEALthy Brain Child Development Study

A longitudinal observational study that aims to understand normative neurodevelopment from birth to 10 years with an emphasis on providing information on the impact of *in utero* exposures to potentially harmful substances and environments.



EEG for baseline, auditory evoked potential, visual evoked potentials, and face-object ERP task



Substance and other risk and protective factor exposures

Behavioral, observational, and neurocognitive assessments

MRI for structural, diffusion, resting state connectivity, and MR spectroscopy





Wearable biosensors for heart rate (HR), HR variability, sleep/wake cycles, and physical activity



Biospecimens for substance use, genomic, epigenomics, nutrition, toxins, and COVID-19



Support for HBCD





HEALthy Brain and Child Development Study



HEALthy Brain and Child Development Study



Conclusions

- The ABCD study is doing well! Retention is high and it is yielding rich longitudinal data.
- The HBCD study has committed to the same open science framework as ABCD providing access to information about early life experiences.
- Together HBCD and ABCD will help to answer questions about neurodevelopment from birth to age 20.
- The ABCD dataset is available to you now, and we strongly encourage you to consider working with it. The first release of HBCD data is anticipated in 2025!

Thank you!



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Questions?