HEALthy Brain and Child Development Study

Michelle Freund, NIDA
CRAN Council
May 10, 2023
What is HBCD?

- A prospective longitudinal study recruiting in 2nd trimester of pregnancy – following through ages 9-10
- Multi-modal assessments of brain, cognitive and emotional development, including influence of substances and environments from birth through childhood
- Characterize neurodevelopmental trajectories from large sample (~7,500 dyads)
- Determine how substance exposure and other environmental factors affect developmental trajectories
- Valuable resource; large dataset will be broadly shared with annual releases
25 Research Sites

UC San Diego
Cincinnati Children’s Hospital
Children’s Hospital Los Angeles/USC
University of New Mexico
Cedars Sinai
Arkansas Children’s Hospital
Boston Children’s Hospital
Northwestern
University of North Carolina
Penn State
University Of Maryland
Children’s Hospital of Philadelphia
*University of Minnesota

University of Vermont
Oregon Health Sciences University
Oklahoma State University
New York University
Vanderbilt
University of Florida
Emory University
Hopkins/Kennedy Krieger
*Washington University
University of Alabama
University of Wisconsin, Madison
HBCD Study Aims

• What are typical neurodevelopmental trajectories and what is the normal range of variability in brain development from birth through childhood?
• How do biological and other environmental exposures affect these developmental trajectories?
• How do genetic influences interact with environmental factors to influence neurodevelopment and cognitive, emotional, and social behavior?
• How does early life exposure to opioids, other substances, and/or other adverse environmental circumstances affect developmental trajectories?
• Are there key developmental windows during which the impact of adverse environmental exposures (e.g., stress, COVID-19) influence later neurodevelopmental outcomes?
• Are there key developmental windows during which ameliorating influences (e.g., substance use disorder treatment; social/economic support) are protective against the potential neurodevelopmental insults of early adverse exposures?
• What is the impact of early parent/caretaker interactions with their children on later health and other outcomes?
Sampling Design

• Need To Accomplish Both Internal And External Validity

Descriptions of developmental trajectories

Questions regarding substance use effects on child health and developmental trajectories

Questions regarding other exposures and/or effect modifiers on child health and developmental trajectories

External Validity / Generalizability

Representativeness of results to target population
  • intermediate target: local source population
  • ultimate target for consortium: US population

Internal validity

Ability to make causal inference (from observational data) by minimizing bias and confounding
Goal 1: 7500 pregnant women (300 women in each of the 25 sites)

Goal 2: 25% (1,875 total or 75 per site) of whom report or have biomarkers indicative of substance use during pregnancy

Goal 3: To recruit a study population that reflects birthing women ages 15-49 in the US (2020 US Census)

Goal 4: To recruit women similar to those who used substances during pregnancy to ensure reasonable balance of potential confounders and improve the internal validity for scientific questions of substance use during pregnancy and child development
Visit Structure Considerations

• Ability to address the Study Aims
• Estimation of trajectories, including impacts of various factors, including:
  ▪ Time-invariant (e.g., genetics, prenatal environment)
  ▪ Time-varying (e.g., family environment)
  ▪ Mediators (e.g., neurodevelopment)
• Good (longitudinal) coverage of the entire 0-48 months age span
• Facilitate statistical analyses without undue complexity
• Enough flexibility to maximize data collection and retention
Child Cognition and Neurodevelopment

Pre-pregnancy Factors
- Maternal Health
  - Substance-use
  - Trauma
  - Perceived Stress
  - Protective Factors

Social and Environmental Determinants
- Early Life Stress
  - Environmental Exposures
  - Poverty
  - Discrimination
  - Access to Resources

Biological Factors
- Physical Health
- Genetics
- Nutrition
- Epigenetics
- Microbiome

Parent/Child Factors
- Child-Caregiver Relationship
- Behavioral Regulation
- Mental Health
- Home Environment

DEVELOPMENT
Remote assessments will take place at visits 5 (10-17 months), 7 (16-50 months), and 8 (36-60 months).
Visit 1

Assessments

Health V1
Timeline Follow Back
ASSIST V1
Demographics V1
APA Level 1 DSM5 Severity Acute Stress or PTSD
APA Level 2
PACES (Current)
BFY – Benefits/Services, Economic Stress
PROMIS Perceived Stress/Social Support
Edinburgh Postnatal Depression Scale
Personal and family psychiatric history
PhenX+ Discrimination
eHITS
PhenX+ Neighborhood Safety/ Geocode

Biospecimens

Blood, urine, saliva (maternal)
Visit 2

Assessments

- MAP-TL, Version: Infancy (< 1 year)
- APA Level 1
- DSM5 Severity Acute Stress or PTSD
- APA Level 2
- PROMIS Perceived Stress/Social Support
- Edinburgh Postnatal Depression Scale
- Breast Feeding History
- 2-Item Food Insecurity
- Participant Feedback Form- Main Study
- Health V2
- Timeline Follow Back
- ASSIST V2

Biospecimens

- Child - urine, stool, saliva
- Birth parent – saliva, nails

Protective Factors
Available Resources
Risks/Stressors
Vulnerability Factors
Parental Health
Parental Mental Health
Infant Health

Anthropometrics

Infant height, weight, head circumference

Wearable Biosensors

Child (sent home, wear 72 hours and return) to measure sleep cycle, activity, heart rate

MRI

- Structural (T1/T2)
- Diffusion, Functional, Quantitative MRI
- MR Spectroscopy

Abstraction from obstetric and birth records
Visit 3
Assessments

SPM-2 Infant
IBQ-R Very Short Form + Behavior Inhibition
MAP-TL, Version: Infancy (< 1 year)
APA Level 1
ASSIST V3
DSM5 Severity Acute Stress or PTSD
APA Level 2 PROMIS Perceived Stress/Social Support
Edinburgh Postnatal Depression Scale
ecPROMIS (<1 y/o) - Caregiver Child Relationship Scale
Breast Feeding History
2-Item Food Insecurity
ERICA
NIH_BTB Cognitive/Executive Function/Memory
NIH_BTB Language

Biospecimens
Child - urine, stool, saliva
Birth parent – saliva

Anthropometrics
Infant height, weight, head circumference

Wearable biosensors
Child (sent home, wear 72 hours and return) to measure sleep cycle, activity, heart rate

MRI
Structural (T1/T2), Diffusion, Functional, Quantitative, MR Spectroscopy

EEG
Baseline, Auditory Oddball, VEP, Faces

Protective Factors
Available Resources
Risks/Stressors
Vulnerability Factors
Parental Health
Parental Mental Health
Infant Health
Infant Behavior
HEALthy Brain and Child Development Study

Number of Consented Parents and Children

Parents 345
Children 244
Race/Ethnicity of Pilot Participants

Race/Ethnicity:
- AI/AN
- Asian
- Black, African American, or African
- Hispanic, Latino, or Spanish
- Middle Eastern or North African
- White
- None of these fully describe me

HBCD Targets:
- AI/AN
- Asian
- Black/African American
- Native Hawaiian and Other Pacific Islander
- Other
- Two or more races
- White
MRI Protocol - Visits 2 and 3

- T1, T2 structural MRI
- Resting fMRI
- Diffusion MRI
- qMRI
- MRS
Pilot EEG data collection

The EEG team evaluates the data for quality. Updated 5/2/2023
Wearable Technology Visits 2 & 3

Movement Sensors

- Visit 2
  - Passed
  - Failed

- Visit 3
  - Passed
Pilot Biospecimen Collection

Biospecimen by Type

Biospecimens Received @ Sampled

Opioids Alcohol Cannabis Nicotine Stimulants

Positive for use on the TLFB Positive Biospecimen

Positive Biospecimen Positive for use on the TLFB Positive Biospecimen and Positive for use on TLFB
Preliminary analysis of pilot samples

**HBCD pilot N = 63**

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**National Positivity rate N ~ 1500**

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Questions?