INFANT BRAIN IMAGING STUDY

Winter 2023/2024

We Need Your Help!

The IBIS sample (now over 1000) is unique in the world. We are extremely grateful to your family for participating. We desperately need your help in finding more families to participate in order to expand this groundbreaking research.

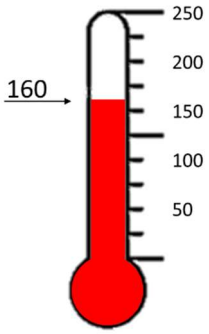
Our studies focus on early infant brain and behavior development in autism, Down Syndrome, and Fragile X. This work has already had a huge impact on the field in informing about prediction of later autism in infancy. We strongly believe that our findings and current research have the potential to transform how we think about, screen for and ultimately treat autism.

But … this work is critically dependent on having enough families with infant children participate**. We need your help in recruiting for the two studies below. Please follow us on social media and re-share; tell your friends and others**. If you have ideas to recruit families, write us at **ibis@wustl.edu**.

Autism:

We are recruiting infants under 6 months who have an older full sibling with autism.

Goal: 250 new babies



Connect and share on social media:

ibis_network

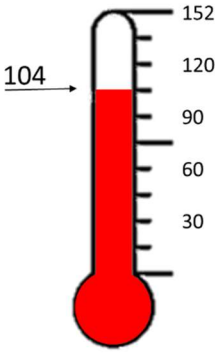
IBIS.Network

https://ibis-network.com/infant/

Down Syndrome:

Recruiting infants under 6 or 12 months who have Down syndrome.

Goal: 152 new babies



Connect and share on social media:

dsstudies

dsstudies

https://dsstudies.com/

A Cellular "Time Machine" to Understand Autism

The IBIS study found that many individuals with autism spectrum disorder exhibit larger brain volumes early in life. A new project of the IBIS Network, called IBIS-iPSC, seeks to find out what causes the increases in brain volume. We think that changes in the way the brain forms, during prenatal development, produce more cells and lead to bigger brains in those individuals that go on to develop autism.

How can we model prenatal brain development in participants from IBIS given that they've already passed the age we are interested in studying? Induced pluripotent stem cells or iPSCs are a way of changing (or reprogramming) blood cells from a given individual in order to "go back in time" and be like the embryo from that individual. From those iPSCs, we can add certain compounds to differentiate them to be little balls of cells that are like the prenatal brain, called cortical or brain organoids.

Since 2019, we've been asking IBIS participants to participate in this study by getting a blood draw. We've had over 110 individuals participate so far with blood draws. We recently received a $4.6M National Institutes of Health (NIH) grant to conduct this work. So far, we have generated cortical organoids from 18 IBIS participants. These little balls of cells form the expected cell types present in the prenatal brain and function in some of the ways we expect, like forming structures that are present in the developing human brain.

In addition, the Pediatric Neuroethics Lab led by Dr. Kate MacDuffie at Seattle Children's Research Institute interviewed 32 parents and adult children in IBIS who have already participated in the blood draw about their attitudes towards research with iPSCs and brain organoids. The results of this interview study were published in Stem Cell Reports. Along with participants who had donated blood or skin samples for research on other neurodevelopmental or neurological conditions, participants in IBIS shared their support of brain organoid research to advance human health. Interview participants also shared that they wanted ongoing engagement with their research teams, for three main reasons: 1) to know about the results of the research they donated to, 2) to have the ability to change who has authority over their donation over time (e.g., to transfer authority to their child once he/she turned 18), and 3) to be able to provide permission or at least be notified if their samples continue to be used past the original goals of the study. These insights from participants in IBIS and related research studies will be incorporated into the design of new strategies for engaging with donors of biospecimens to brain organoid research.

We'd still like to recruit more individuals to participate in the blood draw for the iPSC project to be sure we have a large number of participants to make confident conclusions. Talk with your local IBIS recruiter to join our study if you are interested.

When Autism and Down Syndrome Meet

Drs. Rebecca Grzadzinski and Heather Hazlett were recently interviewed about the intersection of autism and Down syndrome. You can listen to this interview on YouTube.

This interview was hosted by the Down Syndrome Resource Foundation (www.dsrf.org) which publishes the LowDOWN Podcast covering important topics for families related to DS. Topics range from the latest research, self-care, employment, advocacy, and other health issues. Check out all of their podcasts and other resources for families.

The LowDOWN
A Down Syndrome Podcast

Down Syndrome Resource Foundation

Podcast Link
https://www.dsrf.org/resources/the-lowdown-podcast/

IBIS Researcher Spotlight: New Grants

Several IBIS Researchers were awarded new grants this year. These types of grants from the National Institutes of Health, called "K" awards help early career investigators launch their careers, while also answering important research questions. In the IBIS network, we were lucky to have three of our researchers receive a K award this year. Each of their research projects, which is described below, will further expand the work that IBIS is doing to understand early development in autism and Down syndrome.

IBIS investigator, Dr. Casey Burrows, is driven to improve early identification of autism spectrum disorder (ASD) in females. She has been using innovative new data-driven methods to account for sex-based bias in diagnostic instruments in the IBIS sample, which has identified more early autism-related concerns in girls than was previously seen. Her new career development award from the NIH, titled *Towards Equitable Early Identification of Autism Spectrum Disorder in Females,* will extend this work to children screened through primary care with the goal of identifying ASD risk profiles that can be clinically actionable in practice. This work will help identify new screening practices that will lower the age of identification of ASD-related concerns in females.

Casey Burrows, PhD, LP
Assistant Professor, Pediatrics
University of Minnesota

Dea Garic, PhD
Research Assistant Professor
UNC-Chapel Hill

Cerebrospinal fluid (CSF) pathophysiology has been associated with impaired clearance of neuroinflammatory proteins, (e.g., amyloid-beta) and implicated in neurodegenerative disorders such as Alzheimer's disease, but the role of CSF dynamics in neurodevelopmental disorders remains unknown. Dr. Garic's K01 Career Development Award aims to address this gap by elucidating and contrasting trajectories of CSF characteristics in Down Syndrome (DS) and related disorders (autism spectrum disorder and Fragile X syndrome) across the first two years of life, to determine the relationships between CSF physiology and later neural and clinical features. Given that 50% of children with DS will go on to develop early-onset Alzheimer's, CSF physiology can serve as a mechanistic pathway to aberrant brain and behavioral development and has the potential to guide the design of targeted therapeutics for early intervention.

Individuals with Down syndrome (DS) have heterogeneous developmental outcomes and varying support needs which impact quality of life and contribute to significant family stress and financial burden. Identification of objective early markers of specific outcomes that affect everyday life is key for advancing interventions for DS. This study will integrate collection of physiological arousal metrics (cardiac, respiratory, and pupillary dynamics) into IBIS in order to better understand how infants and toddlers with and without DS react to social and non-social stimuli and ultimately learn from their multisensory environment. Ultimately, this project will yield physiological biometrics of arousal that are objective, present in infancy, and provide clinically actionable targets for treatment in early life to ultimately lead to improved outcomes for those with DS and their families.

Rebecca Grzadzinski, PhD
Research Assistant Professor
UNC-Chapel Hill

IBIS Now Following Kids through Adolescence

The Infant Brain Imaging Study (IBIS) Network recently received a grant from NIH to follow forward the wonderful families in this study, as their participating child becomes an adolescent. The goal of this study extension is to examine trajectories of brain and behavior development, from infancy to now extend through to adolescence. We will be inviting subjects from across all IBIS Network locations to return to our sites to participate in what we hope will be an exciting and important addition to our work to date. Participation will include developmental testing, as well as an MRI scan while watching a movie or show of their choice, or during natural sleep. Families and their teen participant will be reimbursed for all travel related expenses and be compensated for this visit. Families can contact the IBIS Network location where they are participating, to find out more information. We will be reaching out to all our families over the coming months to discuss the scheduling of your visit.

We are really looking forward to seeing all our IBIS families again soon!

New Peer-Reviewed Research from the IBIS Network

Predicting self-injurious behavior at age three among infant siblings of children with autism
https://pubmed.ncbi.nlm.nih.gov/37439184/

Association of Sex With Neurobehavioral Markers of Executive Function in 2-Year-Olds at High and Low Likelihood of Autism
https://pubmed.ncbi.nlm.nih.gov/37140923/

Language exposure during infancy is negatively associated with white matter microstructure in the arcuate fasciculus
https://pubmed.ncbi.nlm.nih.gov/37060675/

Sensory Profiles in Relation to Later Adaptive Functioning Among Toddlers at High-Familial Likelihood for Autism
https://pubmed.ncbi.nlm.nih.gov/37017863/

Quantifying latent social motivation and its associations with joint attention and language in infants at high and low likelihood for autism spectrum disorder
https://pubmed.ncbi.nlm.nih.gov/36222317/

Infant Visual Brain Development and Inherited Genetic Liability in Autism
https://pubmed.ncbi.nlm.nih.gov/35615814/

A Data-Driven Approach in an Unbiased Sample Reveals Equivalent Sex Ratio of Autism Spectrum Disorder-Associated Impairment in Early Childhood
https://pubmed.ncbi.nlm.nih.gov/35965107/

Infants later diagnosed with autism have lower canonical babbling ratios in the first year of life
https://pubmed.ncbi.nlm.nih.gov/35761377/

Examining the factor structure and discriminative utility of the Infant Behavior Questionnaire-Revised in infant siblings of autistic children
https://pubmed.ncbi.nlm.nih.gov/35485579/

Subcortical Brain Development in Autism and Fragile X Syndrome: Evidence for Dynamic, Age- and Disorder-Specific Trajectories in Infancy
https://pubmed.ncbi.nlm.nih.gov/35331012/

Are early social communication skills a harbinger for language development in infants later diagnosed autistic?-A longitudinal study using a standardized social communication assessment
https://pubmed.ncbi.nlm.nih.gov/37168581/