

UNC FRAGILE X RESEARCH NEWSLETTER

SUMMER 2021

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ONGOING STUDIES

Following-up on school age children with fragile X who participated in our study as infants

No two children diagnosed with fragile X have the same clinical needs. This variability in fragile X symptomology from patient to patient has greatly hindered clinical treatment trials. Part of this variability is likely due to how the fragile X genetic mutation interacts with the thousands of other genes in the genome, or one's *genetic background*.

The goal of the current study is to better

understand how genetic background, measured

using heritable traits in family members, helps us understand brain and behavior development in children with fragile X from infancy through school-age.



MEET THE TEAM

Jessica Girault, PhD



Dr. Girault is an Assistant Professor of Psychiatry at UNC Chapel Hill who works at the Carolina Institute for Developmental Disabilities. Dr. Girault is the lead researcher on this study and is an expert in infant brain development. Her work focuses on how genetics influence brain development and function in neurodevelopmental disorders.

Lindsay Mullin, B.A.



Lindsay is the project's study coordinator. She schedules study participation and conducts questionnaire interviews with parents in this study. She received her bachelor's degree in developmental psychology with a minor in neuroscience in 2017, and worked in research at Boston Children's Hospital before coming to UNC.

Heather Hazlett, PhD



Dr. Hazlett is a Clinical Psychologist at the UNC Carolina Institute for Development Disabilities. Dr. Hazlett led the original infant fragile X study and is a clinical expert in fragile X syndrome and autism.

In this study we will enroll families of children with fragile X who participated in our original imaging and behavior study as infants and are now between the ages of 6 and 12 years. This remote study will involve a one-time phone or video interview with a researcher, online questionnaires, and at-home saliva DNA collection. Families will be compensated up to \$150 for taking part in this study.

For more information or to participate in the study please email Family_Study@unc.edu or call the study coordinator, Lindsay Mullin, at (919) 966-3594.

To learn more about our study funded by the Foundation of Hope, please visit [our website](#).

Recruiting a new cohort of infants with fragile X

Researchers at UNC School of Medicine and the Carolina Institute for Developmental Disabilities were recently awarded a 5-year, \$1 million grant from the U.S. National Institutes of Health to study the early brain development of babies with Fragile X syndrome. Previous studies by our team have shown that infants who develop autism have abnormally excessive volumes of cerebrospinal fluid (CSF) surrounding the brain (Shen et al., [2013](#); [2017](#); [2018](#); [2018](#)). This excessive amount of CSF was detectable using noninvasive MRI scans by 6 months of age, prior to autism diagnosis, and before the onset of behavioral symptoms.

In this new study, we will be recruiting a cohort of babies with FXS to determine the relationships between CSF measured by MRI, and brain and behavioral development – comparing FXS to autism and other neurodevelopmental disorders.



Babies with FXS will undergo an MRI brain scan starting at 6 months of age, with a follow-up visit at 24 months of age. Brain scans will be conducted with noninvasive MRI during natural sleep (no anesthesia or sedation). The child's behavioral, cognitive, and motor abilities will also be assessed, and these clinical and MRI reports will be returned to the parents and the child's care providers. The goal of this research is to understand the earliest detectable neurological biomarkers in FXS to improve early detection and potential treatments.

All travel costs to Chapel Hill, NC will be covered by the study – including airfare, hotel, rental car, and meals. Families will be compensated up to \$200 for participating in this study. For more information or to participate in the study, please email ShenLab@unc.edu or call the study coordinator, Julia Gross, at (919) 966-8032.

To learn more about this study or other research studies conducted by our lab, please visit our website: markshenlab.org.

MEET THE TEAM

Mark Shen, PhD



Dr. Shen is an Assistant Professor at the UNC Carolina Institute for Developmental Disabilities, Dept. of Psychiatry, and Neuroscience Center. He serves as the Principal Investigator for this study, is an expert in identifying early biological markers for neurodevelopmental disorders, and has acquired hundreds of MRI scans on babies during natural sleep.

Julia Gross, B.S.



Julia is the study coordinator for the new FXS brain imaging study, will serve as the primary point of contact for participating families, and will lead the families through each study visit. Julia has extensive experience working with children with neurodevelopmental disorders and is interested in pursuing a career in neuropsychology.

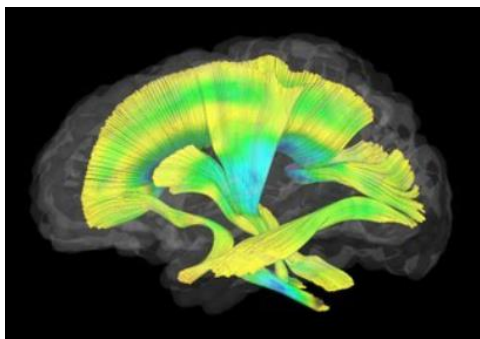
Dea Garic, PhD



Dr. Garic is a Postdoctoral Fellow at the UNC Carolina Institute for Developmental Disabilities. Her current work is centered on identifying early neural features associated with the pathogenesis and symptomatic progression of neurodevelopmental disorders. Dr. Garic will help analyze the data from the MRI scans and behavioral assessments from this study.

RESEARCH HIGHLIGHTS

Brain differences in fragile X are detectable by six months of age



For the first time, UNC School of Medicine researchers used MRIs to show that infants with fragile X syndrome had less developed white matter compared to infants of the same age without the genetic condition. White matter is the underlayer of the brain, beneath the gray matter, and it contains the signaling pathways that connect different regions of the brain. White matter is critical for information flow needed to carry out actions and behavior.

This study highlights that brain differences related to fragile X syndrome are established well before diagnosis is typically made at age 3 or later. Dr. Meghan Swanson, co-lead author of the study, said that “It is our hope that earlier diagnosis and intervention will help children with fragile X and their families.” She also notes that findings from this study may inform drug development research. So far, drug clinical trials have failed to demonstrate change in treatment targets in individuals with fragile X. One of these challenges has been identifying good markers of treatment outcome.

Co-senior author and PI of the NIH funded study, Dr. Heather Hazlett, said, “One of the exciting things about our findings is that the white matter differences we observe could be used as an objective, quantifiable physiological marker to evaluate treatment effectiveness.”

This study was published in [JAMA Psychiatry](#) in 2018.

Boys with fragile X have different brain structure than boys with autism during toddlerhood

Nearly one third of boys with fragile X will meet diagnostic criteria for autism spectrum disorder. Dr. Hazlett and her colleagues designed a study to determine whether overlapping symptoms related to similarities in brain structure, or if autism symptoms in boys with fragile X, had a different neurobiology.



In a study of 18- to 42-month-old boys with fragile X and boys with autism (without fragile X), the researchers found that while boys with fragile X and boys with autism both had enlarged brains during toddlerhood. These overall enlargements were the result of different changes in underlying regional volumes. Specifically, boys with fragile X had enlarged caudate nuclei, a region shown to play a role in the planning of motor movements and in cognition more broadly.

This work was an important step for towards understanding that while autism and fragile X share behavioral symptoms, they have distinct brain features that have important implications for treatment.

This study was published in [*The Journal of the American Academy of Child and Adolescent Psychiatry*](#).

Behavioral differences in fragile X syndrome are evident across the first two years of life

A major focus of our group's research is to differentiate the development of children with FXS from other neurodevelopmental disorders, including autism. We have recently compared the behavioral and cognitive development of FXS infants (from Dr. Hazlett's study above) with infants who develop autism from the Infant Brain Imaging Study (IBIS), as well as typically developing control infants. By 6 months of age, the infants with FXS had significantly lower scores (compared to the other groups) on cognitive ability – which include receptive and expressive language, visual/sensory integration, and fine motor ability. When these new findings are published, we will circulate the publication in a subsequent newsletter.



We want to thank all of the families for their participation in our research. We couldn't do what we do without families like yours! We are excited to be following up with your families to learn more about fragile X syndrome from infancy through childhood.



SCHOOL OF MEDICINE

Carolina Institute for Developmental Disabilities