2017 Update

The team at the Translational Psychophysiology and Assessment Laboratory (T-PAL) is excited to share with you updates regarding the current research being conducted within our group and how your participation in our research projects is helping to advance the world’s knowledge of fragile X syndrome, Down syndrome and other forms of intellectual disability, autism spectrum disorder, and the fragile X premutation.

**Trajectories and Markers of Change in Carriers of the Fragile X Premutation**

(Fragile X carriers are individuals with the FMR1 premutation, who at risk of developing a neurodegenerative condition called fragile X-associated tremor/ataxia syndrome (FXTAS) in later life. FXTAS symptoms include tremor, balance problems, cognitive changes, and a range of other neurological problems. This study co-directed by Dr. David Hessl and Dr. Susan Rivera, aims to discover genetic, brain and cognitive factors that may precede or occur with the onset of FXTAS in adult male fragile X carriers. This is the first longitudinal study of this population. We study intellectual function, motor function, executive function, memory, dexterity, and balance, as well as learn about participants’ psychological health. The brain health portion of our study is completed through magnetic resonance imaging (MRI). Information gathered from these scans includes size, shape, and integrity of the brain and its structures. We also measure brain activity via changes in blood flow as participants complete different cognitive tasks. As we begin the fourth year of our study, we continue to focus on bringing participants back for their second and third visits, and we have enjoyed getting to know them over time. We have learned a great deal about the structure of white matter in the brain, aspects of social cognition (and in some cases, autism-related traits), anxiety, and age-related patterns of changes in brain structure. We especially look forward to taking a closer look at the longitudinal data in the coming year. We know that many of these men and their family members have questions about the premutation, especially how to identify early signs of neurodegeneration and most importantly how to treat or prevent FXTAS. While this is not a treatment study, it will provide extremely valuable information about the natural course of aging in these carriers that will inform treatment studies, and we are working hard with Dr. Hagerman and others to identify the most promising interventions to investigate. Our study will also help to develop and validate clinical or neuroimaging methods that could be used to track effectiveness of these interventions.)
A Cognitive Test Battery for Intellectual Disabilities
(supported by the National Institute of Child Health and Human Development)

The purpose of the “Toolbox” study is to develop and validate an assessment battery to measure cognitive outcomes in clinical trials of individuals with intellectual disability. Specifically, we are validating the National Institute of Health’s Toolbox Cognitive Battery, working with children, adolescents and young adults with fragile X syndrome, Down syndrome, autism spectrum disorder and other forms of intellectual disability. This is a collaboration of centers at Rush University Medical Center (Chicago), University of Denver, Northwestern University and UC Davis. We finished several preliminary studies and published our work in Journal of Neurodevelopmental Disorders (https://jneurodevdisorders.biomedcentral.com/articles/10.1186/s11689-016-9167-4), showing the battery’s potential by virtue of its feasibility, reliability and validity in a group of children, adolescents and young adults with these disabilities. After finishing the pilot phase of the project in the fall of 2015 we began the much more ambitious validation study in February of 2016 with a target of 450 participants across centers. Now that is has been over a year since the validation study’s start, we have recruited over 70 participants at the MIND Institute and another 120 have been enrolled at the Rush and Denver sites. Because this is a longitudinal study, the participants will be returning two years after their initial visit; we will be studying the ability of the Toolbox to measure changes in cognitive development. As more and more investigators in our field move to develop treatments to improve functioning of people with cognitive deficits, we anticipate that our work will help establish new and sensitive methods for tracking these important treatment-related changes.
Cognitive Training for Fragile X Syndrome
(supported by The John Merck Fund)
We are nearing the end of this exciting, 4 year project! This study is a randomized controlled trial to examine the efficacy of a working memory training program to improve cognitive function and behavior in children and adolescents with fragile X syndrome. Thanks to support from the John Merck Fund, we have had the amazing opportunity to travel to 100 families throughout North America! Parents work with their children on a web-based training game 5 days a week, for 5 or 6 weeks; we perform assessments prior to and following training, as well as at a follow-up visit 3 months later. We also collect information on child behavior from parents and teachers. This is a blinded study, meaning we do not know which children received which level of training. We are close to unblinding the study and performing analyses that will help us learn a great deal about whether and how children with fragile X can benefit from an intensive cognitive training program. We are especially grateful to the parents and children who have dedicated so much of their time and effort to this important project.

Extending Autism Behavioral Intervention to Young Children with Fragile X Syndrome
(supported by the National Fragile X Foundation and MIND Institute)
The Early Start Denver Model - FXS (ESDM-FXS) study is a small pilot project which aims to determine whether a well-validated autism behavioral intervention is also effective for young children with fragile X syndrome. ESDM is a parent-delivered intervention where parents learn specific techniques they can use at home during play and daily caretaking routines to help their child learn to speak, play, and interact more with others. Four families participated in this small study and received six months of the therapy from Dr. Laurie Vismara either at the MIND Institute or at home through video conferencing. All four families have completed the study and we are excited to be currently analyzing the data. Preliminary findings suggest that the intervention may help reduce problem behaviors, increase spontaneous communication, and increase joint attention gestures such as shared eye contact and smiles. Larger controlled studies may be conducted in the future to get a clearer picture of how this treatment may work for young kids with FXS and what kinds of modifications might be useful.

Fragile X Clinical and Research Cooperative Consortium Registry and Repository
(FXCRC FORWARD; supported by the National Fragile X Foundation and the Centers for Disease Control)
The MIND Institute is excited to be participating in the National Fragile X Foundation’s FORWARD fragile X study and the fragile X national registry, supported by the CDC. The study is a collaboration between the NFXF and 24 participating fragile X clinics, and aims to improve the care and quality of life of those with FXS. FORWARD looks at the development of FXS over the life span and examines the impact of interventions and treatments. Additionally, the project facilitates FXS research by connecting researchers and families to studies at fragile X clinics around the United States. Participation in the study consists of registering in the database, completing parent questionnaires, and giving permission for medical, psychological, and behavioral data to be entered into the database. Currently, almost 300 individuals are participating at the MIND Institute and over 2,800 individuals are participating in the study nationwide. For a summary of the study’s preliminary findings, please visit the FORWARD website at forwardfx.org.