Title: Uncapping the Possibilities in FXS: A Guide to Successful EEG Collection

Authors: Nicole Friedman1, Nicole McCoy1, Danielle Chin1, Grace Leonardi1, Debra Reisinger1, Rebecca Shaffer1,2, Ernest Pedapati1,2, Elizabeth Berry-Kravis3, Craig Erickson1,2, Lauren Schmitt1,2

1Cincinnati Children’s Hospital Medical Center; 2University of Cincinnati College of Medicine, 3Rush University Medical Center

Introduction: Fragile X Syndrome (FXS) is the leading genetic cause of inherited intellectual disability and autism spectrum disorder (ASD), yet there remains no therapy that can reverse its core pathogenic mechanisms and provide symptom relief. Identification of translational biomarkers in FXS is critical to the enhancement of disease understanding and advancement of behavioral and pharmaceutical treatment development. Electroencephalography (EEG) is the measurement of electrical activity produced by your brain cells when they communicate, using sensors that sit onto of your head. Compared to other brain imaging measures, EEG is relatively non-invasive can be used safely down with any age, even infants, and can be completed in parallel studies of mouse models of FXS. The knowledge gained thus far from EEG studies has provided crucial insight into underlying pathogenic mechanisms, including findings of excitatory: inhibitory imbalance and disrupted neural circuit systems. Despite the clear benefits of using EEG in studies of FXS, behavior challenges and sensory hypersensitivities often interfere with data collection. Thus, we offer behavior-based solutions to improve collection success rate and, we provide two case study examples to demonstrate our successes.

Method: All research coordinators complete behavioral management training conducted by licensed clinical psychologists. A variety of behavioral management strategies grounded in evidence-based techniques are implemented prior to and during EEG collection. Prior to study visits, coordinators complete questionnaire with families to learn about the participant and to share behavior practice guide with parents to begin desensitization at home. Additional behavioral supports are provided to families prior to and during visits, including visual schedules, social stories, token boards, and timers. Each of these are individualized to the participants’ specific needs and interests. During the session, coordinators and psychologists employ a variety of evidence-based behavior techniques as well as creative solutions to other challenging behaviors. Across two funded studies (U54 Fragile X Center (adolescent/adult population) and NN107 FX-LEARN (young child population)), we collected data regarding success rates of EEG collection for each task. Then, we examined success rate based on age and key clinical variables.

Results: Overall, we have very high rates of EEG completion in individuals with FXS across the lifespan at our site at Cincinnati Children’s Hospital. Approximately 88 percent of adolescents and adults and 70 percent of young children had successful EEG data collection on their first try. Successful EEG completion rates also increased over time following subsequent exposure. In our adolescent and adult populations, we found that participants who were able to successfully complete EEG tended to have higher verbal IQ, but otherwise the groups demonstrated fairly similar clinical features. However, irritability seemed to be a distinguishing factor in terms of EEG success in this age group; individuals who were unable to complete EEG tended to score higher on the ABC FXS irritability scale. In contrast, in young children we found no significant clinical differences between the children who were able to complete EEG and those who could not. Of note, we found a decline in successful EEG collection in this age group when visits became less frequent and there was lack of exposure to EEG for multiple months at a time.

Discussion: Most of our current techniques for EEG collection are geared towards easing anxiety and becoming acquainted with the sensory aspects of EEG. Since we found irritability to be a significant factor in EEG success among adolescents and adults, we will work to expand our aids and techniques to help reduce irritability during sessions since these strategies may differ from those used to help with anxiety. We will also continue to explore how our behavioral techniques may have had varying success among our young children population with certain strategies being more effective for sub-groups of children who score similarly on clinical measures (e.g. hyperactivity vs anxiety). We also hope to incorporate practice sessions with EEG caps for young children at more visits throughout their study participation so that we can maintain their comfortability with EEG and increase our EEG success after longer breaks. We are encouraged by our results indicating that patient-focused behavioral interventions not only allow our participants who have an enjoyable experience, but also help us learn more about FXS. Ultimately, by doing
our best to make the EEG data collection experience more enjoyable, we can increase our EEG completion success which helps pave the way to develop new treatments.

References: