**Symposium Title:** Bringing the Laboratory to Homes and Communities: Leveraging PANDABox to Enhance Access to Early Developmental Surveillance Research

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**Discussant:** Susan Rivera³

**Overview:** Effectively assessing early features of neurodevelopmental disorders is critical to facilitating access to early intervention and monitoring the outcomes of both interventions and clinical trials. Telehealth-based screening and treatment options have been increasingly recognized as a pathway to improving clinical access for underserved populations, with most telehealth-based clinical research to date focusing on clinical (e.g., parent interviews) and behavioral (e.g., video observations) methods that are feasible to implement using commercially-available platforms. However, telehealth has been less frequently used to collect data using what we describe as spectral methods: traditionally laboratory-based assessment techniques that capture behaviorally-anchored, high-density spatial or temporal characteristics of participant responses not detectable through observation alone. Indeed, spectral methods such as eye tracking, facial coding procedures, and biosensor assays typically require high quality, tightly synchronized data streams that are difficult, if not impossible, to obtain via commercial teleconferencing software. In addition, these methods are often administered by trained laboratory staff rather than caregivers, making translation to home-based data acquisition challenging. Importantly, however, spectral methods are also commonly hailed as the most objective and sensitive metrics for predicting and detecting early features of atypical development including ASD (Walsh, Elsabbagh, Bolton, & Singh, 2011) and monitoring acute changes over the course of clinical trials (Berry-Kravis et al., 2013; Jeste, Frohlich, & Loo, 2015). As such, developing integrated, scalable telehealth-based protocols for collecting clinical, behavioral, and spectral data remains a critical need that, if satisfied, has potential to radically expand the quality and scope of research in neurodevelopmental disorders.

To address this challenge, Kelleher and colleagues recently developed PANDABox (Parent-Administered Neurodevelopmental Assessment), a caregiver-facilitated, remotely administered assessment protocol for collecting high quality, laboratory-grade data relevant to a wide array of research questions in clinical populations. The present symposium describes the development of PANDABox and its application in a national sample of children with neurogenetic syndromes (Paper 1; Kelleher). We then discuss recent efforts to scale PANDABox to novel populations and contexts, including developmental surveillance of infants with the FMR1 premutation and fragile X syndrome detected through newborn screening (Paper 2; Okoniewski) and international efforts to apply PANDABox tasks to monitor early cognition in infants with congenital Zika syndrome in Brazil (Paper 3; Toth). Across talks, we will discuss the benefits and challenges of using a centralized, telehealth-based protocol to assess early development in special populations, including issues of validity and generalizability, access for underserved populations, rigor and reproducibility, and scalability and cost. Together, we aim to facilitate discussion of whether and how PANDABox and similar telehealth-based research protocols can be optimized to improve assessment, treatment, and subsequent quality of life for children with neurodevelopmental disorders and their families.

**References/Citations:**


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Paper Title: PANDABox Feasibility and Data Quality in a National Sample of Children with Neurogenetic Syndromes

Authors: Bridgette L. Kelleher1, Taylor Halligan1, Nicole Witthuhn1, Wei Siong Neo1, Lisa Hamrick1, Leonard Abbeduto3, & Don Lynam1

Introduction: Optimizing telehealth-based protocols for remote collection of integrated, laboratory-grade data has potential to enhance the quality, scope, and representativeness of neurodevelopmental disorder research and treatment. However, to date, no standardized, open-science option is available. To meet this need, we developed PANDABox, a telehealth-based, caregiver-facilitated, customizable protocol for monitoring early developmental features. In this paper, we describe the process of developing PANDABox using a sample protocol that integrates multiple levels of measurement—clinical, behavioral, and spectral—to assess early developmental features in infants and toddlers. We then present pilot data from three cohorts of children with Down syndrome, Angelman syndrome, and fragile X syndrome. Groups were selected to ensure PANDABox was appropriate across varied levels of developmental delay and medical comorbidities (e.g., low muscle tone, strabismus, seizures), which may affect how children engage in assessment tasks. Here, we focus specifically on (1) logistics and cost, (2) caregiver fidelity and satisfaction, and (3) data quality.

Methods: Reported data are drawn from 16 caregivers and their infants with Down syndrome, and final data will include data currently being collected from children with fragile X syndrome (n=12) and Angelman syndrome (n=12). Although PANDABox is a modular battery that can accommodate a variety of tasks, we report data from a subset of tasks that assessed attention, language, motor skills, temperament, and atypical behaviors. Families were recruited nationally via Facebook support groups and foundation registries. PANDABox kits included all technology (computers, heart monitors, vocalization recording devices) and manipulatives necessary for the assessment. Kits were mailed to families prior to a pre-scheduled assessment window. For each session, the examiner used commercially-available software to remotely access the participant computer, display prompts and stimuli, and coach the caregiver to administer the tasks in real time. After the assessment, the caregiver shipped the kit back to our laboratory, where behavioral and physiological data were synchronized and coded by trained research assistants. Caregivers also completed pre- and post-assessment surveys that assessed technology literacy and assessment feedback, respectively.

Results: Preliminary data indicate PANDABox required low resources to administer and produced cost-savings for data collection rates of seven assessments/month or greater. PANDABox was well received by families, with high caregiver fidelity (94%) and infant engagement (91%). Post-assessment survey data suggested positive experiences, with 97% of responses rated as “good” or “excellent” and 0% of responses as “poor” across items related to satisfaction with assessment materials, ease of technology, duration, examiner support, and privacy. Slightly lower satisfaction was reported for the assessment’s ability to capture the child’s typical behavior, with 7 of 11 “good” or “excellent” responses. Missing data rates were low for video frames (3%) and vocalization recordings (6%) but were higher for heart rate (25% fully missing, 13% partially missing) and discrete behavioral presses (8% technical issues; 19% not enough codable behavior), reflecting the increased technical demands for these activities.

Discussion: The present study provides an initial step toward validating telehealth-based laboratory research sessions to monitor early development in neurodevelopmental disorders. Our findings suggest that with support, caregivers are capable of collecting high-quality, research-grade data with minimal data loss. Relative to clinic-based administrations that require travel, telehealth-based PANDABox administration was projected to be more cost effective at a modest rate of assessment. Moreover, we were able to integrate clinical, behavioral, and spectral data offline, providing a nuanced framework for investigating multiple layers of responses—such as psychophysiological and high-density time-series data—that are more complex than previously reported in telehealth-based research. Looking forward, our goal is to further enhance the applications and scalability of PANDABox, potentially providing a cost-effective, open science platform for the research community to conduct laboratory grade assessments remotely. With proper optimization, our hope is that PANDABox may be particularly beneficial in connecting researchers and patients from underserved communities, including in rural areas. Although substantial development and validation will be needed to achieve this goal, PANDABox may provide a scalable method for collecting higher-powered, lower-cost, and more representative neurodevelopmental data from low-incidence clinical populations.
Paper Title: Piloting the use of PANDABox in Infants with Fragile X

Authors: Katherine C. Okoniewski, Anne Wheeler, Heather Hazlett, Heidi McNeilly, Leigh Anne Weisenfeld, Anne Edwards, & Bridgette Kelleher

Introduction: Individuals with a FMR1 mutations are at risk for a spectrum of involvement including fragile X syndrome (FXS), developmental delay, cognitive impairment, attention regulation difficulties, and autism symptomology; however, there is limited understanding of how these needs progress from infancy. As part of an innovative screening research pilot program in North Carolina, Early Check is offering parents the opportunity to screen their infant for FMR1 full and premutations. Given the wide spectrum of involvement as well as the prevalence of premutations, remote developmental assessments are a necessary aspect of follow up in order to provide adequate surveillance. In order to meet these needs, PANDABox has been integrated into the systematic developmental surveillance and follow-up protocol, with the aim of expanding the application of PANDABox procedures and supporting feasibility and validation initiatives in populations of infants with rare neurogenetic disorders.

Methods: Parents of infants identified with an FMR1 full or premutation were offered the opportunity to participate in follow-up developmental assessments at 3- and 6-months of age using PANDABox and an in-home validation assessment. Utilizing PANDABox's behavioral and spectral measures of attention, temperament, language, and play, participants are administered the following activities through parent guided procedures: 1) attention to infant-appropriate video, 2) free play, 3) arm restraint, 4) bubble and key play, 5) story time, and at 6-months 6) parent-child interaction. Approximately 2- to 4-weeks after completion of PANDABox, validation measures are administered including the Bayley Scales of Infant and Toddler Development, 3rd Edition, Vineland Adaptive Behavior Scales, 3rd Edition, and the Infant Behavior Questionnaire, Very Short Form. After PANDABox completion at 6-months, participants complete an exit survey reflecting on the ease of usability, strengths, weaknesses, and acceptance of the tool.

Results: To date, four infants with the premutation and two with a full mutation have enrolled in the PANDABox pilot. Five have completed PANDAbox and corresponding validation measures at 3- and 6-month timepoints. All parent administrators were mothers who also had a premutation or in one case, a full mutation. Preliminary results indicate acceptance of the protocol, a preference for the ease of use and flexibility, and a willingness to recommend the study to others.

Discussion: Utilizing the innovative procedures afforded by PANDABox provides an opportunity to offer ongoing developmental surveillance to infants and families who may be traditionally underserved or whose prognosis is uncertain. This presentation will offer a glimpse into the use of these remote developmental assessment tools to monitor the very early development of infants with an FMR1 mutation in a noninvasive parent-empowering way. Implications for researchers and clinicians will be discussed.

References/Citations:


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Paper Title: Using Pandabox to Understand Developmental Strengths and Weaknesses in Children with Congenital Zika Syndrome

Authors: Danielle A Toth, Anne C. Wheeler, Camila Ventura, Bridgette Kelleher, Gabrielle Bonanno, Lucélia Lima Nobrega, Raine Costa Borba Firmino, Claudia Marques da Silva, Liana Ventura, Don Bailey

Introduction: Congenital Zika Syndrome (CZS) encompasses a pattern of defects related to in utero exposure to the Zika Virus, including microcephaly, ocular abnormalities, congenital contractures, subcortical calcifications, and hypertonia. Many children with CZS continue to exhibit multiple disabilities and severe impairment across all domains of development, and their motor and visual complications limit the ability to capture their emerging skills and developmental needs with existing measures. For example, results from the first Bayley Scales of Infant and Toddler Development (BSID-III) administration among a cohort of 177 children with CZS (mean age 31.9 months) indicate that about 85-93% of children are scoring at the floor of the measure. However, a wide range in raw scores suggest that some of the children might have skills not captured in BSID-III scores or by other clinical assessment tools. Recognizing the need for novel approaches to more comprehensively understand the developmental strengths and weaknesses of children with CZS, we piloted the use of PANDABox to gauge whether these behavioral and spectral measures could more effectively measure attention among these children. In this presentation, I will discuss the suitability of the use of PANDABox with a cohort of children with CZS, and results from a pilot study measuring attention in children with CZS using heart rate defined sustained attention (HRDSA) as a proxy.

Methods: PANDABox was translated to Brazilian Portuguese and constructs were refined for appropriateness and efficacy for the CZS cohort. Approximately 102 children ages 23-46 months with CZS in Recife, Brazil took part in the attention and social tasks while wearing an FDA-approved eMotion Faros heart monitor. The assessment protocol included 1) a passive viewing task to characterize HRDSA patterns in children with CZS, 2) a name response task to identify within-child difference across experimental conditions of a social cognition task, and 3) a 10-minute mother-child interaction task to understand dyadic processes. All assessments were videotaped and analyzed by a team of trained research assistants. The outcome variable measured was average change in heart rate during the tasks, with greater heart rate deceleration associated with greater sustained attention. QRSTool and CardioEdit were used to extract interbeat intervals (IBIs) and measure heart rate variability.

Results: Preliminary results reveal the average heart rate deceleration of a child with CZS is greater in response to hearing their mother’s voice versus the examiner’s voice in the name response task, indicating the child exhibits more focused attention when hearing their caregiver’s voice. Initial results suggest differential patterns in response to stimuli in their environment even when looking behaviors did not indicate this response. Additional data on the remaining sample are being analyzed and within-individual and within-group differences will be presented.

Discussion: Measuring sustained attention using HRDSA allows us to quantifiably assess children with CZS’s responses to their environment; an otherwise difficult measurement due to impairments that limit visual or physical responses and patterns expressed in typically developing children. Using HRDSA as a proxy measure may provide opportunities to better design behavioral treatments based on cognitive development outcomes measured with tools like PANDABox.

References/Citations:


Altino Ventura Foundation