Symposium Title: Remote delivery of behavioral intervention for ASD: challenges, successes, and considerations moving forward

Chair: Carly Hyde[1]

Discussant: Connie Kasari[1]

Overview: While behavioral intervention is currently the gold-standard for autism treatment, various factors, including geographical dispersal and travel expense, lack of trained professionals and long waitlists, a parent's availability during business hours, and stay-at-home restrictions due to the ongoing COVID-19 pandemic make high-quality interventions challenging and sometimes impossible to access. Telehealth models are a promising way to disseminate empirically validated behavioral interventions to communities. This symposium surveys four preliminary efficacy trials of remote delivery methods in children with neurodevelopmental disorders. The first presentation will examine parent engagement and feasibility of two alternative versions of a web-based reciprocal imitation training (RIT). The second presentation will address parent engagement and monitoring in a video-conference based parent-mediated training for children at high risk for autism due to Tuberous sclerosis complex. The third presentation will discuss the efficacy of a remote play-based intervention for children with Prader-Willis Syndrome. The final presentation will demonstrate the feasibility, fidelity, and acceptability of a pilot remote intervention for Fragile X Syndrome. Collectively, these presentations will address the challenges and successes of remote behavioral interventions, as well as considerations moving forward in the era of telehealth.

Paper 1 of 4

Paper Title: Parent engagement in a self-directed vs. therapist-assisted telehealth program for families of young children with autism spectrum disorder (ASD)

Authors: Allison Wainer[2], Ph.D., Zachary Arnold[2], B.A., Caroline Leonczyk[2], Ph.D., Sarely Licona[2], B.A., Edith Ocampo, B.A.[2], Latha Soorya[2], Ph.D.

Background: There is strong empirical and theoretical support for parent involvement in interventions for autism spectrum disorder (ASD) and related neurodevelopmental disorders, with corresponding growth in the development and evaluation of manualized parent-mediated early interventions (PMI). Despite purported benefits of PMI, such programs are highly under-utilized in community settings, due in large part to a lack of trained professionals, lengthy waitlists, child care, transportation, and reimbursement issues. These barriers compel examination of alternative service delivery methods, such as telehealth, to increase access to care. Benefits of telehealth include greater provider and patient coverage and opportunities for standardized yet individualized learning. Indeed, telehealth is well-suited to deliver interventions with different levels of support depending on the specific needs of an individual and family. While self-directed programs have strong potential for dissemination and a large public health impact, the extent to which therapist-assistance or "coaching" influences program engagement and outcomes remains largely unknown. Our group developed a telehealth program, Mirror Me, to teach families of young children with ASD an evidence-based naturalistic developmental behavioral intervention called reciprocal imitation training (RIT). Mirror Me uses video modules to introduce the intervention strategies and was designed to be used in either a self-

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directed or therapist- assisted format. A goal of this pilot randomized control trial was to determine differences in parent engagement between the self-directed and therapist-assisted formats of Mirror Me.

Methods: This 10-week pilot RCT compares two different formats of Mirror Me: self-directed to therapist-assisted. Participants include 21 families of young children, ages 16 to 49 months, with a diagnosis of autism spectrum disorder and deficits in social imitation skills. All families used the self-directed website for five weeks and then were randomized to continue on their own or receive remote therapist-assistance in the form of "coaching" once per week over the subsequent five weeks. Participants attended in person study assessment visits at baseline (pre-intervention), 10-weeks (post-intervention), and 15-weeks (follow up). Parent engagement with the website, intervention and study assessments was tracked across the active treatment and follow up phases.

Results: One hundred and thirty young children and families were screened over the phone for interest and eligibility in the current study. Twenty-eight enrolled in the study, with 21 (75%) meeting eligibility criteria. Of those 21, four families withdrew during the initial five weeks of the trial, while another three withdrew during the second five weeks of the trial. None of the nine families who withdrew had been randomized to the coaching condition. On average, parents rated Mirror Me as highly acceptable, relatively easy to use, and easy to "see" and "explain to others" the benefits of the program. However, the seven families who withdrew reported "feeling uncertain," having difficulties finding the time to use the website, and challenges determining how to prioritize Mirror Me with respect other concurrent services and interventions. Follow up interviews indicated that for those families who withdrew, initial enthusiasm was dampened by experiencing a lack of support and feeling overwhelmed upon receiving an ASD diagnosis.

Discussion: Results from this pilot study suggest that integration of support, in the form of remote therapist-assistance, may be beneficial for increasing sustained parental engagement with telehealth interventions. Identifying optimal timing and format of remote therapist assistance will be an important next step, along with understanding characteristics that might indicate which families are most likely to require that support. These lines of research will help build a foundation for the development of more adaptive and personalized approaches to telehealth.

Paper 2 of 4

Paper Title: An evaluation of compliance and parent perception for remote early-intervention for tuberous sclerosis complex (TSC)

Authors: Carly Hyde[3] BS, Nicole McDonald[3] PhD, Shafali Jeste[3] MD

Introduction: Tuberous sclerosis complex (TSC) is a rare autosomal dominant disorder caused by mutations in the TSC1 or TSC2 gene, occurring in 1 in 7000-13,000 children (Ebrahimi-Fakhari D et al. 2018). TSC is highly penetrant for autism, with diagnostic rates approaching 60% (compared to up to 2% in the general population) (Jeste et al. 2015). Due to the geographic dispersal and complex medical needs of children with rare genetic disorders such as TSC, remote parent-mediated behavioral intervention is a promising avenue of research (Hyde et al. 2020). As intervention procedures move into the home, it is critical to identify new strategies to monitor parent engagement and their perception of the therapy to continually ensure high-quality administration by parents. In the ongoing JASPER Early Intervention for Tuberous Sclerosis Complex (JETS) clinical trial, we developed a system of

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automated text messaging, online questionnaires, and video submission monitoring to track engagement across the intervention. Here, we 1) evaluate compliance with tools designed to monitor parent engagement, 2) determine parent engagement and perception of change over the course of the intervention and 3) examine how child, family, and logistic factors interact with parent perception of change.

Methods: For all participants (N = 24), compliance with the remote intervention system was evaluated using daily text messages, weekly questionnaires, and video uploads. The Parent Adherence to Treatment and Competence Scale, a parent-report questionnaire administered to caregivers via email each week of treatment, contributed to a rating of perception of change (1 indicating they do not see changes in their child and 5 indicating they see strong changes in their child). Overall response rate for daily text messages and weekly online questionnaires contributed to a composite engagement score. Bivariate correlations and chi square tests were used to determine differences in perception of change and engagement based on child characteristics (seizure status and medical stability, level of autism symptoms, cognitive and adaptive scores), caregiver variables (overall distress, difficulty with scheduling, and daily hassle), and logistic factors (distance from site, income, and hours spent in outside intervention).

Results: Overall compliance the intervention protocol was adequate. The average individual response rate was 75% for text messages and 68% for online questionnaires, and 92% completed the full 12 weeks of intervention. Overall engagement averaged at 75%, and the overall perception of change was high (8.5/10). Parents who reported a high perception of change tended to receive fewer outside interventions ($p = .049$) and reported fewer difficulties scheduling assessments ($p=.007$). Parents with higher levels of engagement tended to be further from the testing site ($p=.047$), and their children were more medically unstable ($p=.028$).

Discussion: Remote delivery will continue to allow families with rare genetic disorders to engage in intervention and clinical trials regardless of the ability to travel, which may remain limited through COVID-19 and beyond. Overall, this system of parent monitoring was tolerable for parents, and produced informative data on parent engagement and perception of change. This data will inform future adaptations to the intervention design such as streamlining online and phone-based metrics to enhance compliance to study protocol. When considering parent reporting (a key component of remote intervention), it is critical to consider the impact of parent perception of change, as well as potentially influential factors. Those with more at stake (higher time and financial investment due to travel distance, access to fewer local services, and more severely impacted children) may perceive greater change in their children over the course of intervention. Further, engagement and perception of change may relate to parent and logistic factors, rather than the characteristics of the child.

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Paper Title: Show Me What Happens Next! Efficacy of a Pilot Study of Remote Play-based Intervention for Children with Prader-Willi Syndrome

Authors: Ellen Doernberg[4], BA, Anastasia Dimitropoulos[4], PhD, Olena Zyga[4], PhD, Sandra Russ[4] PhD

Introduction: Prader Will-Syndrome (PWS) is a rare congenital genetic neurodevelopmental disorder characterized by impactful social-cognitive and socio-emotional deficits, related to overall cognitive and behavioral rigidity and impaired adaptive functioning (Dykens & Kasari, 1997; Holland et al., 2003). Additionally, research from the Dimitropoulos Lab has demonstrated that children with PWS, ages 6-9, showed deficits in pretend play ability similar to an age-matched ASD sample (Zyga et al., 2015). However, the addition of a play partner led to significant increases across play-based domains (imagination, organization, and affect in play) for children with PWS (Zyga et al., 2015). In typically developing children, pretend play is related to many positive outcomes, including social awareness, emotion regulation, and idea generation/cognitive flexibility (Bergen, 2002; Lillard, 1993; Hoffman and Russ, 2012; Moore and Russ, 2006; Wallace & Russ, 2015). Therefore, targeting skill building through play in children with PWS may increase socio-emotional understanding and cognitive flexibility, while decreasing rigidity and repetitive behaviors. Developing behavioral interventions for individuals with PWS is faced with the significant challenge of enrolling enough participants for local studies, but telehealth methodology allows for the reduction of barriers such as distance and cost of in-person trials (Wainer & Ingersoll, 2015). Previous reports by our group (Dimitropoulos, Zyga, & Russ, 2017; Zyga, Russ, and Dimitropoulos, 2018) were the first to show the feasibility of a remote play-based intervention for children in the PWS population. This presentation is a follow-up to the previous report on the **P**lay-based **R**emote **E**nrichment **T**o **EN**hance **D**evelopment (**PRETEND**) program for school-aged children with PWS (Dimitropoulos, Zyga, & Russ, 2017), reporting on the efficacy of the intervention in regards to its impact on children's pretend play ability and cognitive flexibility.

Method: The current pilot study evaluated a 6-week play-based remote intervention administered directly to children with PWS, ages 6-12 years, twice a week, for 15-20-minute sessions. Thus far, 18 children with PWS have completed the program, with ongoing recruitment. All participants completed in-person baseline and post-intervention visits, where measures were used to assess children's pretend play skills (the Affect and Play Scale (APS); Russ 1993, 2014) and cognitive fluency/flexibility (the Multidimensional Stimulus Fluency Measure (MSFM); Moran, 1983). During the intervention period, participating children worked individually and directly with their interventionist via videoconferencing software to complete the PRETEND program. The intervention program was adapted from a play-based program aimed at increasing imagination and emotional expression in typically developing children (Moore & Russ, 2008). Interventionists followed manualized procedures to ensure fidelity in targeting specific skills throughout the program.

Results: At baseline, the PWS group fell within the deficient range (1 SD below) as compared to a norm reference group on all 5 original APS variables (Imagination, Comfort, Organization, Affect Frequency, and Affect Categories). Additionally, the PWS group fell significantly below a norm reference group for their performance on the MSFM at baseline. From pre to post intervention, the PWS group made significant changes in their play skills such that core

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elements of their play were in the normative range post intervention. From pre to post intervention, the PWS group also significantly improved in their flexibility and fluency in thought.

Discussion: Results from the current report are the first to support preliminary efficacy of this intervention in school-age children with PWS. Findings confirm that: 1) children with PWS have deficits in pretend play and cognitive flexibility, evidenced by rigid thought patterns (i.e. getting stuck on a topic) and repetitive behavior (i.e. replaying the same storylines), and 2) the remote play-based intervention significantly improved children's pretend play, and positively impacted their flexibility and fluency in thought. A limitation from the present study was the lack of control group for comparison, though current data collection includes a waitlist control group. Results from this pilot study indicate an important new avenue of feasible and accessible behavioral intervention for school-age children with PWS.

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Paper Title: Parent and Infants with Fragile X Intervention (PiXI): Development and Initial Case Series

Authors: Katherine C. Okoniewski[5], Samantha J. Scott[6], Anne Edwards[5], Melissa Raspa[5], Lauren Turner-Brown[7], & Anne C. Wheeler[5]

Introduction: Fragile X syndrome (FXS) is a genetic condition caused by mutation on the *FMR1* gene which compromises the production of the FMRP protein, necessary for healthy brain development. The intersection of expanded carrier testing and innovative newborn screening practices (Bailey et al., 2019) has allowed for earlier identification of infants with FXS. Symptomology associated with FXS has retrospectively been reported as early as 9 months of age in motor, language, and sensory domains (Roberts et al., 2009). Based on the knowledge of early emergence of developmental delay and the longer term sequalae of FXS, our team has developed and is piloting a targeted early intervention program for infants with FXS and their families: Parent and Infants with Fragile X Intervention (PiXI)**.**

Method: The overarching goal of PiXI is to provide developmental and behavioral support for infants with FXS through a two-phase targeted parent-mediated program. Families are eligible to participate if they have an infant under the age of 12 months who was confirmed to have a diagnosis of FXS before the onset of symptoms. Phase I of PIXI is 8 weeks long and involves: 1) providing psychoeducation to parents and families about fragile X; 2) identifying the landscape of needs in the first 6-9 months of life of the child and family; and 3) engaging in parent-child interactive activities to establish a foundation for Phase II. Phase II focuses more intensely on symptoms likely to emerge in the second half of the first year of life. Based on the Infant Start (Rogers et al., 2014) program designed for infant siblings of children with autism, Phase II focuses on parent coaching to increase early social communication skills and address emerging motor delays. It includes 12 core sessions and up to 4 booster sessions to provide consistent intervention up to the child's first birthday. All sessions are delivered remotely with equipment provided by the study team. Fidelity of administration, analysis of barriers and challenges, acceptability of the intervention for families, and initial efficacy through pre-post assessment of developmental skills, autism symptomology, and parent-child interactions are collected during the active intervention and at six-month intervals through the child's third birthday.

Results: To date, participants include seven mother-infant dyads, one mother-father-infant trio, and one foster mother-infant dyad. Of the infants participating, 7 are males (77%). All participants were identified with FXS within the first 6-months of life and received a diagnosis prior to any emerging symptoms. Four of the infants were diagnosed as a result of participation in a voluntary newborn screening program, five were diagnosed at birth due to maternal carrier testing done during pregnancy, two were diagnosed shortly after birth due to an older sibling receiving a FXS diagnosis. Three of nine participants have completed the full PIXI protocol and are actively enrolled in long-term follow-up. This presentation will describe the rationale and challenges in developing a targeted intervention for infants with FXS and summarize initial findings from the first two years of case series implementation.

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Discussion: As the age of diagnosis for young children with neurogenetic conditions is reduced due to increased carrier and newborn screening initiatives, there will be a need for targeted interventions designed to address unique symptoms of those conditions. This presentation will provide an overview of the development of one such intervention, including the perceived successes, as well as the challenges in identifying very early intervention strategies for pre-symptomatic infants and parents who are in the process of understanding and accepting a new diagnosis.

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