RUTGERS

Brain Health Institute

# Rutgers University Center for Autism Research, Education, and Services (RUCARES)

## 1st Annual Autism Conference

October 28th, 2021

Rutgers University Inn & Conference Center

178 Ryders Lane, New Brunswick, NJ, 08901

**October 28, 2021**

**Program Overview**

**8:30 a.m. Introductory Remarks:**
**Gary Aston-Jones, Professor and Director of the Brain Health Institute**
**Matthew McDonald, President and CEO of Children's Specialized Hospital**
**Larry Kleinman, Professor and Vice Chair for Academic Development**

**9:00 a.m.** ***Virtual Developmental Screening: Developmental Risk, Parent Feedback, and Follow-up***
**Presented by: Jill Harris, Amy Norton, Marilyn Lopez, and Caroline Coffield**

Early developmental screening is important as early detection of developmental risk can lead to intervention that improves functional outcomes. Despite guidelines from the American Academy of Pediatrics (AAP) that all children should receive developmental screening by their healthcare provider, this does not always occur. Indeed, inequities exist with delayed identification of developmental risk for children from racial or ethnic minorities or those where English is not the primary language in the home. To address this need, a free community-based developmental screening program, focused on under-resourced communities, was created which converted to virtual format during the pandemic.

Method: Children ages 11-66 months, not previously enrolled in early intervention or with known developmental diagnoses, were targeted and screenings were offered in English or Spanish. Trained screening coordinators administered the Ages and Stages Questionnaire (ASQ) interactively with child and parent. Parents of children ages 16-30 months also completed the Modified Checklist for Autism in Toddlers-Revised (MCHAT-R/F). Feedback was provided and resources shared. Families of children determined to be at developmental risk were contacted one month later to determine if recommendations had been followed and if further assistance was needed. In response to the pandemic, screenings switched from in-person/within community format to virtual format. A subgroup of families was sent a survey to request further feedback about the virtual screening service.

Results: 2723 children were screened in-person and 241 children received virtual screens. More than half were determined to be at developmental risk (52% in-person and 55% virtual). Of those at risk who were reached one month later, more of those seen in-person had followed recommendations versus those seen virtually (63% vs. 50%). Feedback from virtual screening participants is being collected and will be analyzed.

Conclusions: Both in-person and virtual, free developmental screening effectively identified young children at risk who reportedly had not previously been identified. Issues in parent follow up during the pandemic will be discussed. As this model removes financial (and in the case of virtual format, also transportation and child care) barriers to screening, it may be a model for improved access and reduction of inequities in care.

**9:25 a.m.** ***Functional Analysis of Genetic Variations Found in Clinical Exomes of ASD Patients***
**Presented by: Aniket Bhattacharya and M. Chiara Manzini**

Autism Spectrum Disorder (ASD) and Intellectual Disability (ID) represent genetically heterogeneous neurodevelopmental disorders that are often comorbid and caused by single gene mutations of large effect. The involvement of multiple genes, each affecting a relatively few patients, complicates diagnosis. Genome-wide profiling studies often produce an array of ‘variants of uncertain significance’ (mostly missense) which fail to provide clinicians and caregivers with any specific cues for the disease management. We sought to develop a framework to characterize these variations using CC2D1A, a candidate gene for ASD identified through family studies. We included five de novo, missense mutations found in the clinical exomes of three ASD/ID patients (S327L, G441V, V449M, P319L and E910K) and another two (T580I, R886H) that have previously been reported. All four patients were compound heterozygotes (S327L+G441V, S327L+V449M, P319L+E910K and T580I+R886H). CC2D1A contains

unique motifs (four DM14 domains) and acts as a signaling scaffold regulating the PKA-CREB pathway among many others. CC2D1A overexpression increases cyclic AMP levels which activates PKA and leads to CREB phosphorylation. This pathway can be activated by forskolin. We hypothesized that missense variants in the DM14 region disrupt binding and repression of phosphodiesterase PDE4D, a known cAMP scavenger. When wildtype (WT) CC2D1A is overexpressed, PDE4D is repressed leading to an increase in PKA/CREB activity while the missense variants release repression, increasing cAMP degradation and reducing CREB activation. To test this, we cloned and overexpressed them (individually and in patient combination) in HEK293 cells. Overexpression of mutant CC2D1A protein neither affected protein stability nor the survival of the transfected cells at 24 and 48hrs. By employing luciferase reporter assay, we quantified CREB activation 24hrs after transfection with 6hrs forskolin treatment. Compared to the WT, G441V, V449M, P319L and T580I lead to blunted response to forskolin induced CREB activation ($p=0.0313$, N=6-7, Wilcoxon matched pairs signed rank test), suggesting these variants are most likely loss of function. To decipher the stage of the signaling that these mutants disrupt, we are quantifying cAMP levels (ELISA) and characterizing the CC2D1A complex (immunoprecipitation). Our work suggests mutations in the DM14 domain affect CC2D1A binding to PDE4D and disrupts signaling.

**9:50 a.m. POSTER SESSION 1**

*Engrailed 2 Deficiency and 16p11.2 Deletion Result In Maladaptive Avoidance And Motivation Behaviors*
Presented by: Mimi L. Phan, Emanuel Dicicco-Bloom, Benjamin Samuels, Tonia T. Liu, Neeharika Patibanda, and Robert C. Reisler

*Caesarean Delivery Increases Neurodevelopmental Markers in the Male Mouse Brain*
Presented by: Jeremy K. Lessing, Xiaofeng Zhou, Haipeng Sun, Jincheng Wang, Gloria Dominguez-Bello, and Emanuel DiCicco-Bloom

*Matching Vocational Aptitude and Employment Choice for Adolescents and Adults with ASD*
Presented by: Jenna Budge, James Maraventano, Todd Frischmann, and Robert LaRue

*Living Safely with Disabilities or Special Health Needs*
Presented by: Adrienne Robertiello, Miranda Jakubek, Jill Harris, and Kanzah Sarfaraz

*Prevalence and Treatment of Mental, Behavioral, and Developmental Disorders in Children with Co-occurring Autism Spectrum Disorder and Attention Deficit/Hyperactivity Disorder: A Population-Based Study*
Presented by: Myriam Casseus

*Alternative Reinforcer Rate and Resurgence of Destructive Behavior*
Presented by: Shannon Angley, Grace Kurywczak, Wayne Fisher, Ashley Fuhrman, Daniel Mitteer, and Brian Greer

*A Choice-Based Approach for Schedule Thinning Treatments for Multiply Maintained Destructive Behavior*
Presented by: Halle Norris and Brian Greer

*Amygdala Oxytocinergic Neuromodulation in the Visceral Control of Social Behavior*
Presented by: Hunter T. Lanovoi and Ioana Carcea

*A Qualitative Literature Review of Service Needs of Parents of Children with Autism Spectrum Disorder during COVID-19 Pandemic*
Presented by: Hyun-Ju Ju and Debra A. Harley

*Leveraging Massively Parallel Reporter Assays for Characterizing Non-Coding Regulatory Variation in Autism*
Presented by: Justin Koesterich, Anat Kreimer, and Stephan Sanders

**10:40 a.m.** ***The Emotional Support Plan: Preliminary Results From a Brief Telehealth, Mobile Intervention to Support Autistic Adults***
**Presented by: Vanessa Bal, Jacqueline Shinall, Gabrielle Gunin, Emily Istvan, Emily Brennan, and Evan Kleiman**

Background: Autistic adults are at high risk for co-occurring psychiatric conditions, such as depression and anxiety. Difficulty regulating negative emotions may leave them particularly vulnerable during stressful periods, such as the transition to postsecondary education or the COVID-19 pandemic. At present, there are few evidence-based interventions for depression in autistic adults. This presentation will discuss a brief telehealth and mobile intervention called the Emotional Safety Plan (ESP), modeled after similar suicide risk reduction interventions, designed to support autistic adults during stressful periods.

Method: Sixteen autistic adults participated in a study aimed at addressing emotional distress during the COVID-19 pandemic. They participated in a two-session telehealth portion followed by eight brief, weekly monitoring visits to gather information about ESP use and mental health symptoms (PHQ-9, GAD-7). Follow-up interviews were conducted at 8 and 12 weeks.

Results: Satisfaction interview data suggests that the ESP was well-received by participants; on average, participants rated the intervention as helpful, relevant and that they would recommend to others. Reductions in self-reported depressive symptoms were also observed during the eight-week post-intervention monitoring period ($d$=.94 to 1.39).

Discussion: These results provide preliminary support for the ESP to support autistic adults in coping with distress during the pandemic. Results will be discussed in the context of informing ongoing studies utilizing the ESP alongside ecological momentary assessment and with postsecondary students. This presentation will also highlight new partnerships formed between departments at Rutgers and opportunities for future collaboration.

**11:05 a.m.** ***Neural Differences in Social and Figurative Language Processing on the Autism Spectrum***
**Presented by: William Graves, Hillary Levinson, Linsah Coulanges, Shannon Cahalan, Daniel Cruz, Vanessa Bal, and Miriam Rosenberg-Lee**

Individuals on the autism spectrum without language delays or impaired verbal IQ often still have trouble with abstract language, including social and figurative language. Social content is prominent in figurative language, making it challenging to disentangle the source of difficulties in autism spectrum disorder (ASD). This overlap parallels overlapping neural systems for social cognition and language comprehension, including the putative default mode network (DMN), middle temporal gyrus from the anterior (ATL) to the posterior (pMTG) temporal lobe. Taking adjective-noun phrases as the minimal unit in which linguistic context can be employed, we orthogonally manipulated social/nonsocial and figurative/literal dimensions. We hypothesized that the ASD group would show most distinct activation in the social/figurative phrase condition. Additionally, we expected to find brain areas sensitive to one dimension (e.g., figurativeness) or the other (i.e., socialness). Participants were individuals either with ASD (N = 19, mean age = 21.4) or without (N = 22, mean age = 21.3). ASD status was tested with the ADOS-2 Module 4 and verified by a clinician. Groups did not differ in age, IQ, or VIQ. During fMRI, participants viewed a screen and pressed a button to indicate whether or not the phrase displayed was familiar to them. The 192 phrases were divided equally in the 2 x 2 (social/nonsocial x figurative/literal) design. MRI was performed using a Siemens 3T Trio with standard settings optimized for fMRI. Analyses implemented the general linear model and statistical thresholding for whole-brain mapwise correction to $p < 0.05$. Literal > figurative activation occurred in the right pMTG for the NT group only. The only significant group difference was greater deactivation for the NT group in the right ATL for the social/figurative condition. This is consistent with our previous study showing activation for more clearly interpretable phrases in the right pMTG. The lack of difference in ASD suggests these participants were processing the figurative/literal distinction without engaging the standard semantic/DMN network. Consistent with our

hypothesis, the deactivation of the right ATL by the NT group alone suggests the ASD group is not using the DMN/semantic network to process combined social and figurative language.

**11:30 a.m. Jeremy Veenstra-VanderWeele: *KEYNOTE ADDRESS***

**12:30 p.m. LUNCH**

**1:30 p.m. *Transcranial Photobiomodulation (tPBM) is a Non-Invasive Form of Brain Stimulation with Near Infrared Light in ASD Children***
**Presented by: Yuli Fradkin, Eugenia Steingold, Sergey Burd, Michael R. Hamblin, Liza Logounova, Margaret A. Naeser, and Katya Sverdlov**

Objectives: To demonstrate if transcranial photobiomodulation is effective treatment modality to improve language and communication skills in children with autism (ASD).

Background: In recent pilot studies tPBM has been shown to be effective for stroke, TBI, and depression. Furthermore, recently, two small pilot studies showed that tPBM can reduce symptoms of autism. We hypothesized that children with ASD will demonstrate improvement in communication skills and language acquisition with experimental treatment.

Methods and Materials: Our study looked at the effect of tPBM modulation on symptoms of Autism in children 2-6 years old. It is a randomized, placebo-controlled, double-blind study. Currently, 29 out of 30 participants are enrolled. Participants are wearing the tPBM portable device on their head, while playing with toys or engaging in other activities. The treatment is administered in researcher's office. Each participant completes 16 sessions during an 8-week course of the study. Data about children's behavior is collected from parents through weekly interviews. Children's therapists are interviewed regarding any observed changes in child's behavior. Before and after treatment scores of Childhood Autism Rating Scales are compared for placebo and experimental conditions. EEG data from frontal, occipital and temporal area is collected before and after each treatment.

Results: We demonstrated that tPBM could be effective treatment for younger children with ASD and to contribute in improving of language skills . Preliminary CARS results, after completion of 21 subjects show an effect has statistical significance: before: 45.3 ± 5.7 after 35.4 ± 4.7 T-test p-value: 1-sided: p=.0019; 2-sided: p=.00095. EEG changes show decrease in delta waves and increase in alpha beta and theta in few patients which is associated with better focus, implicit learning, and faster language acquisition. Summary of Trajectory of alfa and betta 13.2-15.36-8.78-7.45-21.8-27.7 (increasing), Trajectory of Delta wave 0-31.4-27.8-19.2-27.7-0 (decreasing). Compared to sham, active stimulation presented suppression of the increase in the lower frequency bands (delta) and a further increase in power in the higher frequency bands (alpha, beta,). Normalization of alfa activity can represent normalization of DMN functions and increased organization in cortex, including language areas.

Conclusion: We demonstrated that tPBM is a safe and effective treatment modality for younger children with ASD.

**1:55 p.m. *Autism Spectrum Disorder Screening of Young Children in Newark***
**Presented by: Marisa Palmeri , Jordon Jones, Joseph Schwab, Hanan Tanuos, Claudia Alcindor-Sparman, Shruti Banugaria, Josephine Shenouda, and Walter Zahorodny**

The American Academy of Pediatrics recommends all children be screened for Autism Spectrum Disorder (ASD) at 18 and 24 months-of-age. However, there is a persistent gap between the time of parental concern for ASD and the time of first professional evaluation, particularly in underserved communities. The delay in ASD detection may be related to lack of an effective screener and inadequate follow through with screen positive children. This study will test whether implementing an ASD Screening Program, with the inclusion of peer support for mothers, will increase ASD screening and referral to services through a Newark-based pediatric practice. The ASD Screening Project is an ongoing study initiated in 2020 at the

Rutgers—New Jersey Medical School (NJMS) Pediatric Continuity Care Center (PCCC). Cooperating with the practice physicians, we enhanced routine ASD screening using a new brief and reliable autism screener, the Psychological Development Questionnaire for Toddlers (PDQ-1), for children between 18 and 36-months, followed by liaison on behalf of screen positive children with Mom2Mom, a peer support group. To determine project efficacy, frequency of ASD screening prior to and following initiation of the ASD Screening Project were compared. To date, the project has led to an 18% increase in screening from 2019 to March 2021. Similar increases in the percent of young children (PCCC patients) referred to the local Early Intervention Program (EIP) (68.7% to 93.8%) and to development specialists (43.70% to 75.0%) were observed. These gains were made in 2020/2021, despite the ongoing global pandemic. Despite the apparent success of the project, screening by the PCCC was still less than perfect, reaching approximately 50% of age-qualified children, however, and with post-positive referral to developmental specialists of only 75%. There is room for improvement as well as a need to continue the project in the Newark area and expand beyond it. Incomplete screening and varying referral practices are possible contributors to the lower than expected results. To address these issues, our group is compiling information on ASD screening and referral patterns in New Jersey to gauge where additional screening outreach is needed and provide ASD information to pediatric practices.

**2:20 p.m. POSTER SESSION 2**

*Optimization of ASD Identification Through Use of ATLAS.ti*
Presented by: Lisa Gu and Walter Zahorodny

*ASD Pathogenesis: Modeling the Role of Altered Microbiome in an ASD-Related Mouse Model*
Presented by: Anya Mirmajlesi, Courtney McDermott, Xuesong Zhang, James Millonig, Martin Blaser, and Emanuel Bloom-DiCicco

*Experiences of Latino Families in the First Months Following an Autism Diagnosis of their Young Child*
Presented by: Caroline N. Coffield, Ijeoma Unachukwu, Deborah M. Spitalnik, Jill F. Harris, and Manuel Jimenez

*Early Life Antibiotic Exposure Alters Postnatal Neurogenesis in 16p11.2 Neurodevelopmental Disorder Mice*
Presented by: Courtney R. McDermott, Xuesong Zhang, Xiaofeng Zhou, James H. Millonig, Martin J. Blaser, and Emanuel DiCicco-Bloom

*Caregiver and Self Perception of Quality of Life in Children with Autism Spectrum Disorder and Comorbid Attention-Deficit/Hyperactivity Disorder*
Presented by: Claire M. Marchetta, Myriam Casseus, Joman Y. Natsheh, Anna Malia Beckwith, and Matthew B. McDonald III

*Reduced Hippocampal Inhibition and Enhanced Autism-Epilepsy Comorbidity in Mice Lacking Neuropilin 2*
Presented by: Carol Eisenberg, Deepak Subramanian, Milad Afrasiabi, Patryk Ziobro, Jack Delucia, Michael Shiflett, Vijayalakshmi Santhakumar, and Tracy Tran

*Neural Circuits for Social Behavior Adaptations to Environmental Temperature*
Presented by: Zahra Adahman, Rumi Oyama, Taiga Abe, Justin Riceberg, and Ioana Carcea

*Treatment of Food Selectivity in an Adult with Autism Spectrum Disorder*
Presented by: Whitney Pubylski-Yanofchick, Christopher Manente, Robert LaRue, and SungWoo Kahng

*Abnormal Extracellular Matrix Regulation in an Autism-Linked Mouse Model*
Presented by: Sarah Young and Ozlem Gunal

*Functional Prosody in People with Autism Spectrum Disorders: A Meta-Analysis of Recent Literature*

Presented by: Sten Knutsen and Karin Stromswold

*Efficiently Teaching Adults with ASD in a VR Environment to Safely Navigate Pedestrian Street Crossing*
Presented by: Christeen Scarpa, Cecilia Feeley, Whitney Pubylski-Yanofchick, Dillon Reitmeyer, Christopher Manente, Robert LaRue, and SungWoo Kahng

*Modeling Long-Range Connectivity Deficits in Autism Spectrum Disorders using Cerebral Organoids*
Presented by: Denise Robles, Andrew Boreland, Zhiping Pang, and Jeffrey Zahn

*Perinatal IL-6 Increase Disturbs Secondary Germinal Zone Neurogenesis and Gliogenesis Producing Behavioral Phenotypes Reminiscent of ASD*
Presented by: Fernando Janczur Velloso, Kanzah Sarfaraz, Ekta Kumari, and Steven W. Levison

**3:10 p.m. *Modeling Synaptic Mechanisms of Autism-Associated Neuroligin-3 R451C Mutation Using Human Neurons***
**Presented by: Le Wang, Vincent R. Mirabella, Peng Jiang, Davide Comoletti, Kelvin Kwan, Ronald P. Hart, and Zhiping P. Pang**

Synaptic dysfunction represents a key pathophysiology in neurodevelopmental disorders suchas autism spectrum disorders (ASDs). A mutation, R451C in human Neuroligin 3 (NLGN3, encoded by X-linked gene NLGN3), a cell adhesion molecule essential for synapse formation, has been linked to ASDs. Despite success in recapitulating the social interaction behavioral deficits and the underlying synaptic abnormalities in mouse models, the impact of NLGN3 R451C on the human neuronal system remains elusive. Here, we generated isogenic knock-in human pluripotent stem cell lines harboring NLGN3 R451C allele, a rare mutation found in human ASD patients, and examined its impact on synaptic transmission. Analysis of co-cultured excitatory and inhibitory induced neurons (iNs) with mutation revealed an augmentation in excitatory synaptic strength compared to isogenic control, but not in inhibitory synaptic transmission. Consistently, the augmentation in excitatory transmission was confirmed in iNs transplanted into mouse forebrain. Using single-cell RNA seq on co-cultured excitatory and inhibitory iNs, we identified differentially expressed genes (DEGs) and found NLGN3 R451C alters gene networks associated with synaptic transmission. Gene ontology and enrichment analysis revealed convergent gene networks associated with ASDs and other mental disorders. Our finding suggests that the NLGN3 R451C mutation could preferentially impact excitatory neurons, which causes overall changes in network properties and excitation-inhibition imbalance related to mental disorders.

**3:35 p.m. Ellen Wilkinson: *Identifying Strengths and Positive Qualities of Autistic Adolescents and Adults***
**Presented by: Ellen Wilkinson, Le Thao Vy Vo, Zoe London, Sherri Wilson, and Vanessa Bal**

It is essential to acknowledge that individuals develop new skills throughout childhood and into adulthood (Bal et al., 2018), yet aside from savant skills, there is limited research exploring autistic strengths into adulthood. The current study adds to previous literature by examining parent-reported strengths of autistic adolescents and adults aged 15-30 years with diagnoses of ASD (n=36), Intellectual Disability (ID; n=18), or both (ASD+ID; n=14). Quantitative analysis was performed on parent responses to the prompt, “Please describe the best things about [your child].” Six categories of strengths emerged: Sociability, Personality Characteristics, Interests or activities, Work ethic/motivation, Specific skills, and Other. Almost all parents provided a response (97%), and 3-4 strengths were reported on average. Personality characteristics were most commonly reported, and Sociability was second most commonly reported for the ASD-only and ID-only groups. Specific skills were second most commonly reported for the ASD+ID group. The ASD+ID group was less likely to have a parent-reported Sociability strength ($X^2(2)=5.67$, $p=.05$). Those with ASD (ASD-only and ASD+ID) were more likely to have Specific skills ($X^2(1)=5.28$, $p=0.02$). Analyses identified a new category not covered in previous studies: Work ethic/motivation, which included subcategories capturing a desire to succeed, work ethic, perseverance, and desire to be independent. This new category could be a reflection of the older, transition-age sample. Additionally, it may be surprising to some that Sociability strengths were so commonly endorsed for those with ASD. Upon closer inspection, results revealed that helping behaviors and seeking interaction were the most commonly endorsed

Sociability subcategories. This is an important reminder that while there is often an emphasis on social "skills", prosocial behaviors are additionally important and may be able to support positive interactions. This study is among the first to describe parent-reported strengths and positive qualities of autistic adults. A deeper understanding of individual strengths in adults with ASD and/or ID is important to build supports and foster well-being. Better understanding and identification of strengths of autistic individuals will provide insight into the promotion of good quality of life and contribute to improved public acceptance.

**4:00 p.m. Closing Remarks:**
**Wayne Fisher, Professor and Director of RUCARES**