



RUTGERS

Brain Health Institute

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

2nd Annual Autism Conference

October 26th, 2022

Rutgers University—Busch Student Center
604 Bartholomew Road, Piscataway, NJ, 08854

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Program Overview

8:30 a.m. Introductory Remarks:

Wayne Fisher, Professor and Director of RUCARES
Michael Zwick, Senior Vice President for Research

9:00 a.m. *IMPRoving Expression of Skills and Strengths in Interviewing in a Virtual Environment: The IMPRESSIVE trial in autistic youth*

Authors: **Helen M. Genova**, Mikayla Haas, Heba Elsayed, Michael Dacanay, Matthew J. Smith

Despite many autistic adults expressing a desire to work, nearly 85% of adults on the autism spectrum are unemployed. The autism community has identified that the job interview is a significant obstacle to obtaining employment. A growing field of research has focused on evaluating innovative training tools to improve interview skills. Our previous work shows that a virtual reality job interview training (VR-JIT) tool improves certain job interview skills (such as sounding professional, establishing rapport), but does not improve the ability to speak about personal strengths and abilities. Thus, the current study combined VR-JIT with a new training tool: Kessler Foundation Strength Identification and Expression (KF-STRIDE), an intervention which uses principles of positive psychology. KF-STRIDE targets identification of personal character strengths and expressing those strengths to employers in a socially appropriate way. The current study evaluated effectiveness and acceptability of the combined intervention in 20 autistic youth, randomized to an experimental group (n=10) and a services-as-usual (SAU) control group (n=10). Those in the experimental group participated in a 12 session intervention (9 sessions using VR-JIT and 3 sessions in KF-STRIDE). Each session was roughly one hour. Job interview performance was assessed by video-recorded mock job interviews rated by blinded assessors pre- and post- the intervention. Paired samples t-tests were conducted to examine differences in job interview skills from baseline to follow up in both groups. The intervention group showed a significant improvement from baseline to follow-up in job interview skills in general ($p = .004$), and specifically sharing strengths about themselves to a future employer ($p = .004$). No significant differences were seen from baseline to follow-up in the SAU group. Feedback from those who participated in the intervention indicated high acceptability. The autism population is significantly underemployed leaving these individuals disadvantaged in living independent lives. Two innovative tools: VR-JIT and KF-STRIDE successfully improved job interview skills, including the ability to identify and express character strengths. These findings indicate that these combined tools may help to improve employment skills for individuals on the autism spectrum.

9:25 a.m. *Oscillatory differences in theta and gamma spectral power and phase synchrony may underlie rapid auditory processing abilities in infants with a family history of autism.*

Authors: **Silvia Ortiz-Mantilla**, Teresa Realpe-Bonilla, Cynthia Roesler, April A. Benasich

During the first year of life, typically developing infants can discriminate fast, successive changes in auditory sounds, occurring in the tens of milliseconds range. This rapid auditory processing (RAP) skill is essential to decoding ongoing speech and to the establishment of phonetic maps. Compromised language abilities are ubiquitous in individuals with autism spectrum disorder (ASD), a highly heritable developmental condition. Language delays are already present at 12 months of age in infant siblings of children with ASD, suggesting that prelinguistic processing abilities are compromised. However, the neural mechanisms sub-serving language acquisition in ASD are poorly understood. This EEG-based study investigated oscillatory mechanisms underlying RAP in infants with a family history of ASD (FHA) and matched controls (CT). At 4- months, infants were presented with an auditory oddball paradigm while dense-array EEG was recorded. Infants passively listen to tone pairs separated by a short inter-stimulus interval. Source localization of event-related generators and time-frequency analysis of event-related oscillations at the source level were conducted. A two-dipole model identified sources of activation in the left (LAC) and right (RAC) auditory cortices. We present here preliminary results from a small sample of 6 infants (4 males and 2 females) in each group. Significant oscillatory differences in spectral power and phase synchrony were found between the groups. Specifically, the FHA group exhibited less spectral power for the standard representation in low-gamma in LAC and RAC, mid-gamma in RAC, and high-gamma in LAC compared to the CT group. During deviant discrimination, FHA group showed less power than CTs in theta, gamma, and high gamma in both LAC and RAC sources. The FHA group also

displayed less phase synchrony in the theta range for the standard in RAC and the deviant in both LAC and RAC sources than in CT group. Our preliminary results indicate that RAP is already altered at 4 months in FHA infants and suggest that some of the linguistic differences observed in ASD may arise from variations in oscillatory patterns subserving pre-linguistic processing abilities. Detecting the earliest signs of deviation may be critical for implementing targeted interventions oriented to improving atypical developmental trajectories.

9:50 a.m. POSTER SESSION 1

Incorporating components of brief habit reversal to reduce skin picking and vocal tics in an adult with autism

Authors: Ashley M. Fuhrman, **Shannon M. Angley**, Grace P. Kurywczak, Brian D. Greer

An individualized approach to teaching adults with autism to successfully navigate job interviews

Authors: **Caroline Hatton**, Courtney Butler, SungWoo Kahng

Emotional neurodiversity: The complex emotional lives of autistic adults

Author: **Aaron R. Dallman**

Associations between co-occurring conditions and age of autism diagnosis: Implications for mental health training and adult autism research

Authors: **Nikita Jadav**, Vanessa Bal

Comparing attendance rates for autism spectrum disorder evaluations conducted virtually and in-person

Authors: **Charles S. Borgen**, Danielle Zsamba, Andrew Edwards

Employment related social communication deficits in youth on the autism spectrum

Authors: **Heba E. Elsayed**, Peter Meulenbroek, Jacob Gronemeyer, Zuzanna Myszkowski, Kari Sherwood, Helen M. Genova

Depression and anxiety treatment options for autistic adults: Feasibility and acceptability of two behavioral activation therapies

Authors: **Ellen Wilkinson**, Gabrielle Gunin, Brian Chu, Andrew Jahoda, Richard Hastings, Vanessa Bal

Academic achievement, empathy, and systematizing among college students with and without autism: A preliminary study

Authors: **Chinedu Nkwo**, Roberto A. Abreu-Mendoza, Cory McCabe, William Graves, Miriam Rosenberg-Lee

Prevalence and characteristics of non-verbal and minimally-verbal children on the autism spectrum

Authors: **Celine Molfetta**, Riddhi Vyas, Matthew Conlan, Victoria Vought, Kate Sidwell, Josephine Shenouda, Walter Zahorodny

Leveraging massively parallel reporter assays for characterizing non-coding regulatory variation in autism

Authors: **Justin Koesterich**, Anat Kreimer, Stephan Sanders

Heart rate as a predictive biomarker for severe destructive behavior

Authors: **Liam H. McCabe**, Brian D. Greer

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Research Pathology Services

Center for Advanced Human Brain Imaging Research (CAHBIR)

Preclinical Brain Imaging at Rutgers University Molecular Imaging Core

10:40 a.m. *Linkage between early intervention programs and preschool disability service utilization by children with autism spectrum disorder*

Authors: **Victoria Vought**, Matthew Conlan, Celine Molfetta, Kate Sidwell, Josephine Shenouda, Walter Zahorodny

Early Intervention Programs (EIP) are federally-mandated services for children ages 0-36 months with various developmental delays/disabilities, including Autism Spectrum Disorder (ASD). EIP provide opportunities to learn and practice social interactions and skills prior to entry into the school system. Preschool enrollment qualifies these children for the continuation of services in school under the Preschool Disability (PSD) classification. Despite the benefits of PSD classification, usage among children with ASD is limited. To evaluate how involvement in EIP was associated with participation in PSD, five consecutive cycles (2006-2016) of surveillance by the New Jersey Autism Study were analyzed using the CDC Autism and Developmental Disabilities Monitoring Network methodology. Information on 4050 8-year-old children with ASD from Essex, Hudson, Ocean, and Union counties was analyzed. Demographic covariates, including sex, race, and socioeconomic status, along with the clinical covariates, intellectual disability and degree of impairment, were considered. Pearson Chi-square tests, standard logistic regression models, adjusted odds ratios (AOR) with 95% confidence intervals (CI) were used to analyze data. Among ASD children who received EIP, 88.0% continued to receive PSD services, compared to 46.5% of those who did not participate in EIP ($p < 0.001$). No sex-based differences were observed. Non-Hispanic white children had the lowest PSD usage (63.9%) and non-Hispanic black children had the highest (68.5%) rates of use. Children residing in high-income areas were more likely to participate in PSD compared to children in low-income regions ($p < 0.01$). Children with co-occurring intellectual disability and those with greater severity of impairment had greater odds of PSD classification compared to peers ($p < 0.001$). In adjusted models, children who participated in EIP were 8-9 times more likely to receive PSD services. While differences in birth year and race remained, income was not a significant predictor. Interestingly, county of residence was a significant factor. Compared to children residing in Union County, children in Hudson (AOR: 0.5; CI: 0.4-0.7) and Ocean (AOR: 0.8; CI: 0.6-1.0) counties had 50% and 20% lower odds of receiving PSD services, respectively. Universal ASD screening of toddler-age children may facilitate EIP participation and increase PSD enrollment.

11:05 a.m. *The role of neuropilin 2 in excitatory and inhibitory neuron development, morphogenesis and function*

Authors: Carol Eisenberg, Deepak Subramanian, **Jack DeLucia**, Milad Afrasiabi, Jiyeon Baek, Vijayalakshmi Santhakumar, Michael Shiflett, Tracy S. Tran

During nervous system development, formation of excitatory and inhibitory neuronal circuits establish a delicate balance between excitatory and inhibitory (E/I) synaptic transmission. When brain development goes awry, it often leads to E/I imbalance, which contributes to developmental disorders such as Autism Spectrum Disorder (ASD) and childhood epilepsies. These developmental abnormalities can occur in the embryo (early development), or they can occur after birth (postnatal development) during synapse formation and refinement, and even in the adult when circuit maintenance is required. It is not clear how early and late developmental perturbations differentially contribute to degradation of E/I balance and behavior deficits, such as those observed in ASD. We examine Neuropilin 2 (Nrp2), a cell surface receptor for the semaphorin signaling family of ligands, specifically for the secreted semaphorin Sema3F. Nrp2 is ideal for studying development of E/I balance, because it is expressed both early and late in development and in both inhibitory interneurons and excitatory cortical and hippocampal neurons. Indeed, the SFARI database (score 2) has identified Nrp2 as a strong candidate autism-associated gene variant, consistent with polymorphisms in the human gene locus linking it to ASD. To study the different roles of Nrp2 signaling in developmental E/I balance, we used an inducible *Nrp2* conditional knockout mouse model to selectively delete *Nrp2* in a spatiotemporal manner in hippocampal inhibitory interneurons and found that early (embryonic) *Nrp2* deletion altered cell migration, neuronal activity, cognitive flexibility, and social behavior. In addition, we specifically deleted *Nrp2* in excitatory cortical layer 5 pyramidal neurons during later (postnatal) development and found supernumerary dendritic spine phenotypes similar to those observed in postmortem human brains of autistic patients. Furthermore, we found that Nrp2 can cellautonomously

increase dendritic spine density when it is acutely deleted in adult mouse cortical neurons, suggesting a novel role in circuit maintenance. Taken together, our results provide novel insights into Nrp2's diverse roles in distinct temporal and cell-type specific signaling in excitatory and inhibitory neurons' development required for the proper establishment and maintenance of E/I balance in mammalian brain circuits and behavior output.

11:30 a.m. Kristen Brennand: KEYNOTE ADDRESS

12:30 p.m. LUNCH

1:30 p.m. *Inclusion in innovation – Capacities of virtual and augmented reality to enhance safety of people with autism and other disabilities*

Authors: **Adrienne Robertiello**, Jill Harris

Autistic people are a large and growing population often unprepared for situations that may put their safety at risk or cause injury. The content and format of current safety education typically neglects many safety needs of autistics and others with disabilities.

Study Design: To better understand safety and safety education issues and to develop recommendations for ASD/disability-related safety education and training, we facilitated eleven nationwide *Inclusion in Innovation Summit* brainstorming sessions. The summit was one component of "Living Safely with Disabilities and Special Health Needs," an initiative funded in part by an Inclusive Healthy Communities Grant from the Division of Disability Services, New Jersey Department of Human Services.

Methods: Each summit session, co-led by a disabled advocate and subject matter expert, discussed a previously-identified high impact safety topic: law enforcement interactions, fire safety, elopement/being lost, and recognizing/communicating personal violence and abuse. Invitees nationwide included disabled advocates, emergency responders, researchers, caregivers, educators, and others.

Results: 165 participated. Main points included the need for greater involvement of disabled people in design, implementation, and evaluation of safety education/training; dearth of outcome data on effectiveness of safety education/training; and the promise of Augmented Reality/Virtual Reality (AR/VR) as a training modality. Benefits of AR/VR for people with various disabilities, caregivers, emergency responders, educators, and other safety stakeholders included its immersive nature which allows for safe participation and practice of safety skills including in high risk situations. Additional potential benefits included customization across situations, disability characteristics, and diverse identities, and the ability to measure training effectiveness in real-time.

Potential Impact: This summit informed a whitepaper outlining best practices for inclusive safety education and training through emerging technology and providing a call to action for collaborative research to measure utility, accessibility, generalization of safety skills in real-world environments, and reduction of injuries. Such research could help incite technology developers to address the disabled population. This research has the potential to establish best practices for improving safety and preventing injury for autistics and other disabled people. Further, it could support improved preparedness, response, and mitigation practices for emergency responders. Other resources created within the grant will be reviewed.

1:55 p.m. *Elevated perinatal interleukin-6 modifies synaptogenesis producing ASD-like behavioral phenotypes*

Authors: **Fernando Janczur Velloso**, Sidra Ali, Cynara Sepulveda, Anna Wadhwa, Ozlem Gunal, Steven W. Levison

Epidemiologic studies have demonstrated that perinatal infections and several other maternal immune challenges during pregnancy increase the risk of offspring developing neurodevelopmental disorders that include autism (ASD) schizophrenia, ADHD, depression and developmental delay. However, the mechanisms through which inflammation affects neural development are still not fully understood. Animal

models that aim to reproduce maternal immune activation (MIA) using bacterial and viral mimetics during gestation have shown long lasting behavioral changes in the offspring reminiscent of human neurodevelopmental disorders, including communication, cognitive and social deficits. Animal and epidemiological studies also have implicated inflammatory cytokines as key pathogenic agents. We have shown previously that administering IL-6 to mouse pups on postnatal days 3-6 affects the balance of neural stem cells and neural progenitors in secondary germinal matrices, resulting in fewer neurons, astrocytes and oligodendrocytes being produced in late developing brain structures relevant to the behavioral deficits seen in MIA models. We hypothesized that these cellular deficits may affect synaptogenesis in brain circuits responsible for social behaviors and communication. Using field potential recordings from the Schaffer collateral-CA1 synapses in acute dorsal hippocampal slices from young adults, we found that male mice injected perinatally with IL-6 had strong trends towards both enhanced LTP and LTD, suggesting that IL-6 treatment is potentiating NMDA mediated responses. *In vivo* recordings of the CA1 ventral hippocampus projections to the medial prefrontal cortex revealed reduced post-tetanic potentiation in the IL-6 treated mice, suggesting an effect on short-term plasticity at these synapses. Correspondingly, the IL-6 treated mice had an increased density of spines on the dendrites of frontal cortex neurons, with reduced complexity of those dendrites. Those synaptic changes were accompanied by behavioral deficits classically associated with neurodevelopmental disorders. IL-6 injected male mice lost social preference in both the social approach and social novel subject tasks; they spent ~30% less time socially engaging with sexually receptive females and produced ~50% fewer ultrasonic vocalizations during mating. Furthermore, both male and female IL-6 injected mice engaged ~50% more time in self-grooming behavior. Altogether, these data provide new insights into the biological mechanisms linking perinatal immune activation to complex neurodevelopmental brain disorders.

2:20 p.m. POSTER SESSION 2

Legal decision-makers in cases involving defendants with autism spectrum disorder: A review of research and call to action

Authors: **Carolina R. Caliman**, Colleen M. Berryessa

Deficits in facial memory and metamemory in youth with ASD and ADHD: Implications for self-awareness

Authors: **Marget Whedon**, M. Lewis

Analyses of the autism-associated neuroligin-3 R451C mutation in human neurons reveals a gain-of-function synaptic mechanism

Authors: **Le Wang**, Vincent R. Mirabella, Xiao Su, Ranjie Xu, Peng Jiang, Kevin Y. Kwan, Ronald P. Hart, Thomas C. Südhof, Zhiping P. Pang

Eip participation leads to earlier diagnosis of children with autism

Authors: **Justin Lazzarino**, Walter Zahorodny, Josephine Shenouda, Kate Sidwell

Reading in autism shows enhanced activation of visual association cortex and greater sensitivity to imageability

Authors: **Cory McCabe**, Shannon Cahalan, Melanie Pincus, Mariam Mehboob, Miriam Rosenberg-Lee, William W. Graves

Accounting for environmental and task-specific factors for improving employment matching for adolescents and adults with ASD

Authors: **Jenna Budge**, Robert LaRue, James Maraventano, Todd Frischmann, Sungwoo Kahng

The effects of noncontingent auditory stimulation, response interruption and redirection, and reinforcement on stereotypy and on task behaviors

Authors: **Natalie Riggio**, Kathryn Prozzo, Ingrid Rodriguez, Rachel Davis, Nicholas Migliaccio, Sarah Levine, Daniel Park, Robert LaRue

Modeling long-range connectivity deficits in autism spectrum disorders using cerebral organoids

Authors: **Denise A. Robles**, Andrew J. Boreland, Zhiping P. Pang, Jeffrey D. Zahn

The effects of early life cephalosporin antibiotic exposure on hippocampal neurogenesis in 16p11.2 microdeletion mice

Authors: **Anya S. Mirmajlesi**, Katherine Kimbark, Xuesong Zhang, Xiaofeng Zhou, Courtney R. McDermott, James H. Millonig, Martin J. Blaser, Emanuel DiCicco-Bloom

A novel murine model to study potassium channel-related autism spectrum disorder

Authors: **Alessandro Bortolami**, Elena Forzisi, Irving Estevez, Mladen-Roko Rasin, Federico Sesti

Is EEG could be used for measuring results and monitoring the progress of treatment in ASD study?

Author: **Yuli Fradkin**

The Rutgers University Neurodiversity Taskforce: Assessing current campus climate for neurodivergent students, faculty, and staff

Authors: Christopher Manente, **Giulietta Flaherty**

Early-life antibiotic exposure is associated with dysregulated behavior in genetically vulnerable 16pDel mice

Authors: **Katherine Kimbark**, Anya Mirmajlesi, Courtney R. McDermott, James H. Millonig, Benjamin Samuels, Martin J. Blaser, Emanuel DiCicco-Bloom

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*Research Pathology Services
Center for Advanced Human Brain Imaging Research (CAHBIR)
Preclinical Brain Imaging at Rutgers University Molecular Imaging Core*

3:10 p.m. *Early life antibiotic exposure and genetic risk in neurodevelopmental disorders: Effects on the gut microbiome, neurogenesis, and behavior*

Authors: **Courtney R. McDermott**, Anya Mirmajlesi, Zhan Ghao, Katherine Kimbark, Christiana Ntim, Xuesong Zhang, Xiaofeng Zhou, James H. Millonig, Benjamin Samuels, Martin J. Blaser, Emanuel DiCicco-Bloom

Neurodevelopmental disorders (NDDs) affect the lives of >17% of children in the United States. While genetic factors play a major role in pathogenesis, even identical twins have incomplete concordance, indicating a role for environmental factors. To determine whether environmental factors act through particular genetic susceptibilities to produce distinct NDD outcomes, we investigate a Gene x Environment (GxE) model of NDDs. A recently identified factor that has been linked to increased NDD outcomes is exposure to cephalosporin antibiotics during the first two years of life, when neurogenesis, the process by which neural precursors proliferate, migrate, and differentiate into specialized cells of the brain, predominates. Extensive research indicates that antibiotic exposure decreases the diversity of gut bacteria, which may consequently alter adult brain structure, function, and behavior. However, little is known about effects on neurogenesis, identified as a point of convergence in NDD pathogenesis based on human genetic, postmortem, and animal model studies. Our studies use a novel GxE model to determine how cephalosporin exposure alters postnatal neurogenesis and behavior in the genetically vulnerable 16p11.2 microdeletion (16pDel) mouse. This mouse models one of the most frequently observed copy number variations implicated in NDDs, including ~1% of autism diagnoses. To model antibiotic exposure during infancy, wildtype and 16pDel littermates were exposed to saline (control) or the cephalosporin, cefdinir, from postnatal days 5-9. We hypothesize that early life cefdinir exposure interacts with NDD genetic vulnerability to acutely impact the gut microbiome and postnatal neurogenesis, and selectively dysregulate neurodevelopment and behavior in 16pDel mice. 16S rRNA gene sequencing revealed significant reductions in alpha and beta diversity of cecal samples from cefdinir-exposed mice. We also detected reproducible significant reductions in hippocampal neurogenesis for cefdinir-exposed 16pDel male mice, as quantified by immunoblotting and immunohistochemistry. Lastly, in our first cohort of mice for behavioral studies, we found a significant reduction in sociability for the mice exposed to cefdinir, compared to controls. In conclusion, these data support our hypothesis: exposure to a therapeutic level of a cephalosporin during early life perturbed the gut microbiome, altered behavioral outcomes, and selectively dysregulated neurogenesis in 16pDel male mice.

3:35 p.m. *Clinical symptom outcomes of a brief mobile intervention for autistic adults through the use of weekly and ecological momentary assessment data*

Authors: **Annabelle Mournet**, Gabrielle Gunin, Jacqueline Shinall, Nikita Jadav, Vanessa H. Bal, Evan Kleiman

Introduction: Impaired emotion regulation presents difficulties for autistic adults to adapt to everyday stressors, particularly coping with unprecedented disruptions from the emergent COVID-19 pandemic, yet there is a dearth of interventions to support these mental health needs. Therefore, a brief telehealth and mobile intervention, the Emotional Safety Plan (ESP) was designed to support autistic adults during stressful periods. Utilizing weekly and ecological momentary assessment data, we aim to describe the impact of the ESP on clinical outcomes.

Methods: Fourteen autistic adults developed an ESP and completed 14 weekly and 4x/daily assessments of mental health symptoms and affective states. Linear mixed effect models were used to assess changes in symptoms and to assess if use of specific parts of the ESP since the most recent EMA survey were associated with certain affective states.

Results: For weekly assessments, there was an initial decrease in anxiety symptoms from weeks 1-4 ($b=-3.56$, $p<.001$), with no significant decrease from weeks 4-14. The intervention showed no effect on weekly depressive ratings. Regarding momentary analyses, when participants felt sad during the previous EMA assessment and used the ESP in between assessments, sadness was reduced ($b=-0.18$, $p=.004$). Differential relationships were observed between use of specific ESP sections and subsequent affective states (e.g., use of distractions and coping activities section was associated with feeling relaxed; $b=3.22$, $p<.001$).

Discussion: The ESP had valuable impacts on clinical outcomes. Future research should explore ways to maintain the improvements in clinical outcomes. Such research has the potential to support autistic individuals during times of stress and promote use of healthy coping skills.

4:00 p.m. Closing Remarks:

Wayne Fisher, Professor and Director of RUCARES