



# Fourth Annual

## Dr. Benjamin Goldberg

# Developmental Disabilities

## Research Day

Program and Abstracts

# Presentation Schedule

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- 9:30am      Registration
- 10:00am     Poster Viewing
- 10:55am     Introductory Remarks - Dr. Rob Nicolson and Dr. Julio Martinez-Trujillo

## **Presentations**

- 11:00am     **A Behavioural Observation Scale for Assessing Children's Intelligence Described by the WISC-V.**  
Saklofske, D., & Babcock, S.
- 11:15am     **Sensory Processing in ASD and ADHD: A Multi-Groups Approach.**  
Parks, K.M.A, Schulz, S.E., & Stevenson, R.A.
- 11:30am     **The Role of Interleukin-15/Natural Killer Cells in Maternal Immune Activation's Effects on Offspring Hearing and Behaviour.**  
Haddad, F., Patel, S., De Oliveira, C., Wiczerzak, K., Allman, B. Renaud, S., & Schmid, S.
- 11:45am     **Child and Family Predictors of Timeliness of Autism Identification and Trends Over Time: Implications for Diagnosis Among Girls.**  
McDonnell, C.G., Anagnostou, E., Nicolson, R., Kelley, E., Georgiades, S., Liu, X, & Stevenson, R.A.
- 12:00pm.    **Lunch**
- 1:00pm.     Keynote Address.  
**Next Generation Neurodevelopmental Research in the Clinic and the Classroom.**  
Dr. Daniel Messinger

- 2:00pm **“This Device is Very Important for My Son...” Parents Help Predict the Facilitators and Barriers to Everyday Use of AAC Devices.**  
Servais, M., Ryan, S.E., AlMudullal, M., Shepherd, T.A., & Renzoni, A.
- 2:15pm **A Randomized, Placebo-Controlled Study of Tideglusib in the Treatment of Adolescents with Autism Spectrum Disorder.**  
Nicolson, R., Bennet, T., Thorpe, K., & Anagnostou, E.
- 2:30pm **Fatigue in Cerebral Palsy-Contributing Factors and Management Strategies.**  
Brunton, L.
- 2:45pm Break
- 3:00pm **Studying Sensory Processing using Translational Behaviours in the *Cntnap2* Rat Model of ASD.**  
Scott, K., Mann, R.S., Allman, B.L., & Schmid, S.
- 3:15pm **Traumatic Life Events, Internalizing and Externalizing Symptoms in Children with IDD.**  
Lapshina, N., & Stewart, S.
- 3:30pm **Sensory Processing in ASD and ADHD: A Transdiagnostic Mechanism.**  
Schulz, S.E., & Stevenson, R.A.
- 3:45pm Final remarks and award presentation – Dr. Rob Nicolson and Dr. Julio Martinez-Trujillo

## Keynote Speaker

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### Dr. Daniel Messinger



Dr. Daniel Messinger is a Professor at the University of Miami. He is the Coordinator of the Developmental Psychology Program, the Associate Director of the Child Division (Developmental Program), the Director of the Social Systems Informatics, Center for Computational Science, the Director, UM SIB SMILE, and a Cooper Fellow at the University of Miami.

Dr. Messinger investigates the temporal dynamics of communication to understand how infants and children develop in social relationships. His focus is social, emotional, and language development. Dr. Messinger is a behavioural imager who uses computer vision and other forms of machine learning to objectively measure what children do. He uses computational approaches including time-series analysis and network models to make sense of the big behavioural data that objective measures provide. Dr. Messinger's current work focuses on children with communication disorders. He conducts research with children affected by autism spectrum disorder (ASD) and children with hearing loss. By understanding interaction, Dr. Messinger fosters pathways to healthy development. Specific projects include the emergence of secure attachment, sex differences in the development of autism, and language networks in inclusive classrooms.

Dr. Messinger has experience leading longitudinal research initiatives funded by the National Institutes of Health, the National Science Foundation, and the Institute of Education Sciences. He serves as Coordinator of the Developmental Psychology Program at the University of Miami, and loves talking to prospective developmental graduate students.

## Poster Presentations

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- Poster 1      **Measuring the Meaningful: WHO's International Classification of Functioning, Disability, and Health (ICF) as a Tool to Analyze Measures for a Longitudinal Autism Study**  
Nagee, A., Lakkadghatwala, R., Trinari, E., & Kraus de Camargo, O.
- Poster 2      **Evaluation of a Social Support Program for Children with Down Syndrome and Their Typically Developing Siblings.**  
Amicarelli, A., Miko, J., & Neil, N.
- Poster 3      **Brain Metabolite Dynamics in First-Episode Schizophrenia Using 7.0-Tesla Functional Magnetic Resonance Spectroscopy.**  
Jeon, P., MacKinley, M., Dempster, K., Palaniyappan, L., & Theberge, J.
- Poster 4      **Supporting Treatment Plans for Children/Youth with Developmental Disabilities to Address Factors Associated with Caregiver Distress.**  
McKnight, M., Theall, L., & Stewart, S.
- Poster 5      **Family Dynamics, Trauma, and Child-Related Characteristics: Examining Factors Associated with Co-Morbidity in Children With and Without an Intellectual Development Disorder.**  
Dave, H., Stewart, S., & Lapshina, N.
- Poster 6      **Emotional Face Stimuli Evokes Regionally-Specific Activation in The Amygdala in Adolescents and Adults With Autism Spectrum Disorders.**  
Seguin, D., Chen, J., Nicolson, R., Martinez-Trujillo, J., & Duerden, E.
- Poster 7      **Statistical Learning and How it Relates to Language and Reading Abilities: An Event-Related Potential Study"**  
Moreau, C., Joannise, M., Batterink, L., Liesemer, K., & Isabel, C.
- Poster 8      **Neural Representations of Gaze Direction in Primate Basolateral Amygdala.**  
Mahmoudian, B., & Martinez-Trujillo, J.
- Poster 9      **The Effects of Adolescent Stress on Schizophrenia.**  
Dong, S., & Rajakumar, N.
- Poster 10     **Acoustic Startle Response in Children with Autism Spectrum Disorder with and without Co-Morbidity of Attention Deficit Hyperactivity Disorder.**  
Phillips, R., Schmid, S., & Nicolson, R.

- Poster 11      **Fruits of Genomic Match-Making: De Novo Variants in *PRR12* are Associated with a Wide Spectrum of Eye and Neurodevelopmental Anomalies.**  
Balci, T.B., Wang, L., Lalani, S., Heide, S., Keren, B., Mignot, C., Morley, G., Walia, J., Wheeler, P., Lemons, J., Rodriguez-Buritica, D., Riberi, E., Biamino, E., Schatz, K., Gunay-Aygun, M., Wiesener, A., Zweier, C., Wentzensen, I., Siu, V.M., & Bi, W.
- Poster 12      **Training in Developmental Disabilities in Canadian Psychiatry Residency Programs: Residents Perspectives.**  
O’Flanagan, S., Hallock, S., & Nicolson, R.
- Poster 13      **Violence Against Women with Intellectual Disabilities in Canada: A Systematic Review.**  
O’Flanagan, S., Boldt, G., & Nicolson, R.
- Poster 14      **Neurodevelopmental Outcomes in Infantile Hydrocephalus: An fMRI Case Study.**  
Ahmed Hashi, I., de Ribaupierre, S., & Eagleson, R.
- Poster 15      **Quality of My Life and Fatigue: Perceptions of Boys with Duchenne Muscular Dystrophy and Their Caregivers.**  
Bhullar, G., Wei, Y., El-Aloul, B., Speechley, K., Miller, M.R., & Campbell, C.
- Poster 16      **Health-Related Quality of Life and Fatigue in Children with Duchenne Muscular Dystrophy: A Three-Year Longitudinal Study.**  
Bhullar, G., Wei, Y., El-Aloul, B., Speechley, K., Miller, M.R., & Campbell, C.
- Poster 17      **The Relationship Between Emotion Recognition Ability, Subjective Emotional Intensity, and Traits Associated with ASD.**  
Shafai, F., Gateman, E., Stow, M., Montenegro, J., Abraham, A., & Stevenson, R.A.
- Poster 18      **Does Ventricular Volume Affect the Neurodevelopmental Outcome in Infants with Intraventricular Hemorrhage?**  
Lo, M., Kishimoto, J., Eagleson, R., Bhattacharya, S., & de Ribaupierre, S.
- Poster 19      **Analyzing the Electrophysiological Effects of Rett Syndrome on Neuronal Network Development Using Machine Learning.**  
Khaki, M., Pradeepan, K., & Martinez-Trujillo, J.
- Poster 20      **Modeling Executive Functioning Development in Chinese & Canadian Children: A Novel Mobile Assessment Game Battery Approach.**  
Pham, J., Goldsmith, S., Hampshire, A., & Morton, J.B.

- Poster 21     **Maturation of the Amygdala Subnuclei in children with Neurodevelopmental Disorders**  
Chen, J., Seguin, D., Nicolson, R., Martinez-Trujillo, J., & Duerden, E.
- Poster 22     **Epilepsy Worry in Adolescents and Young Adults with Childhood-Onset Epilepsy: An Exploration Ten Years After Diagnosis.**  
Huang, C.W., Anderson, K.K., Zou, G., & Speechley, K.N.

## Abstracts – Oral Presentations

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### **A Behavioural Observation Scale for Assessing Children's Intelligence Described by the WISC-V.** Saklofske, D., & Babcock, S.

The assessment of intelligence and cognitive abilities is a key factor in the diagnostic evaluation and intervention planning for children with learning and behavioural challenges. It is the manifestation and expression of the child's intelligence that often draws attention to the need for more detailed and exact measurement of general mental ability and its major factors. Teachers and parents are in the best position to observe a child's 'abilities in action' which has considerable importance when determining the need for intelligence testing. In turn, the psychologist can use this information to guide hypothesis formulations regarding cognitive abilities as well as to compare these behavioural descriptions with the results obtained from standardized intelligence tests. The purpose of this study is to identify specific classroom behaviours observed by the teacher to create a 'checklist' that aligns with current cognitive measures used for diagnosis (e.g., WISC-V). The development of this screening tool has so far included qualitative data obtained from focus groups comprised of clinical and school psychology graduate students, practicing psychologists, and an expert panel, and will next include pilot data from children referred for assessment. Validation studies with children referred for psychological testing will then determine the relationship between the checklist behaviours and the WISC-V FSIQ and major factors. This measure will better 'connect' intelligence test scores with behaviors observed by teachers 'in situ' and add a much more detailed and accurate assessment of the child's manifest intelligence together with prescriptive implications.

### **Sensory Processing in ASD and ADHD: A Multi-Groups Approach.**

Parks, K.M.A, Schulz, S.E., & Stevenson, R.A.

**Background:** Children with ASD and ADHD have many overlapping issues, including atypical sensory processing. Despite this, few researchers have directly compared sensory processing patterns in these groups.

**Objective:** To evaluate the validity of the current seven-factor model in describing sensory processing patterns in ASD and ADHD using the Short Sensory Profile (SSP).

**Methods:** Participants included 571 children and young adults (Age range=1.88-21.89, Mean age=10.01±3.98), with ASD (n=361) and ADHD (n=210). Confirmatory factor analyses were performed using individual SSP items on each group with latent variables defined based on the original subscales of the SSP. Subscale scores were then directly compared across groups. Finally, exploratory factor analyses were conducted to examine whether subscale scores clustered differently across diagnoses.

**Results:** For both diagnostic groups, the CFA confirmed the originally proposed latent variables well. However, direct comparisons across diagnoses revealed the ASD group showed greater impairment in tactile, taste/smell, movement, low-energy, and visual/auditory, and the ADHD group showed greater impairment in the auditory-filtering domain. Finally, the EFA revealed that subscales clustered into two categories in ASD (vestibular/movement, sensory-reactivity), but only a single cluster in ADHD (sensory processing).

**Conclusions:** Despite finding that individual items clustered onto the same factors for ASD and ADHD, the scores on the subscales differed. Further, while the items loaded onto the same seven factors across diagnoses, the factors themselves clustered in a different configuration across diagnoses. These findings are useful for understanding the underlying structure of sensory processing in diagnostic groups with similar sensory patterns.

## **The Role of Interleukin-15/Natural Killer Cells in Maternal Immune Activation's Effects on Offspring hearing and Behaviour.**

Haddad, F., Patel, S., De Oliveira, C., Wiczerzak, K., Allman, B., Renaud, S., & Schmid, S.

**Study Objectives:** Maternal infection and its associated immune response during pregnancy are known risk factors for neurodevelopmental disorders such as autism spectrum disorder and schizophrenia in the offspring. Maternal immune activation (MIA) by pathogen-free immune stimulants in pregnant mothers produces brain and behavioral deficits in the offspring related to these disorders. Natural Killer (NK) cells are innate immune cells whose maturation is dependent on Interleukin-15 (IL-15) and are involved in the response to infections. Our study sought to determine the contribution of Interleukin-15 and NK cells on the effects of maternal immune activation, given the association of NK cells with autism and schizophrenia as well as their important immune and developmental role in the placenta.

**Methods:** We induced MIA using the viral mimic polyinosinic: polycytidylic (poly I:C) at gestation day 9.5 in homozygously bred wild type (+/+) or IL-15 knockout (-/-) rats and tested offspring hearing and sensorimotor behaviour in adolescence and adulthood.

**Results:** Our results indicate that IL-15 deficiency reduces hearing threshold and speeds up conduction in the auditory brainstem response regardless of MIA and increases startle reactivity in adolescence. Moreover, poly I:C differentially affected offspring prepulse inhibition, startle reactivity and open field exploration in an age and genotype-dependent manner. For example, poly I:C reduced startle reactivity in adult +/+ but not -/- offspring.

**Conclusions:** Our results point towards a role for NK cells in brain development and MIA mechanisms and further work will attempt to determine whether changes exist in the underlying circuitry for the observed deficits.

## **Child and Family Predictors of Timeliness of Autism Identification and Trends Over Time: Implications for Diagnosis Among Girls.**

McDonnell, C., Anagnostou, E., Nicolson, R., Kelley, E., Georgiades, S., Liu, X., & Stevenson, R.A.

**Study Objectives:** Early identification of autism spectrum disorder (ASD) is an essential healthcare priority because early intervention promotes adaptive long-term outcomes. Although ASD symptoms may be present as early as infancy, diagnosis typically lags far behind. Girls, in particular, may be at-risk for late diagnosis, although research is equivocal regarding how sex and other family-level demographic risk factors relate to ASD identification.

**Methods:** Children (N = 645; 22% female) with a diagnosis of ASD were recruited through the Province of Ontario Neurodevelopmental Disorders (POND) Network. Study records included age of diagnosis (AOD), date of diagnosis (between 1996 – 2017), age of first parent concern (AOC), clinician judgment of symptom onset, demographics, and cognitive testing results.

**Results:** Overall, AOC occurred before age 2 (M=21.44 months) whereas AOD (M=59.36 months) was delayed until about 5 years of age. Girls were diagnosed significantly later and had a longer time between AOC and AOD. Lower family income was associated with later AOC and AOD. Among girls only, lower income was associated with later clinician report of symptom onset. Higher verbal IQ was associated with longer time to diagnosis and later AOD, an association that was significantly stronger for girls. Regarding time-related changes, average AOD increased across the study period, and female sex and verbal IQ exacerbated this effect.

**Conclusions:** Our results support that female sex is a key factor underlying disparities in ASD identification and highlight the urgent need to improve diagnostic practices among females. Implications for reducing healthcare disparities in autism diagnosis are discussed.

### **“This Device is Very Important for My Son...” Parents Help Predict the Facilitators and Barriers to Everyday Use of AAC Devices.**

Servais, M., Ryan, S.E., AlMudullal, M., Shepherd, T.A.(1,5), & Renzoni, A.

**Background:** While functional communication and language skills are fundamental for children to participate in all aspects of life, children with developmental disabilities may face challenges with face-to-face communication. Children whose daily communication needs are not met by natural speech can benefit from augmentative and alternative communication (AAC) systems to support and improve their everyday communication (Cook & Miller Polgar, 2008). However, there are challenges for families and children who use aided AAC systems. Families must learn not only how to operate sophisticated electronic devices, but also how to support their child’s use of the technology to participate successfully in communicative interactions with different communication partners and in different environments (Light, 1997).

**Methods:** This exploratory study used a cross-sectional research design (mailed survey) and regression analysis to identify factors that predict everyday communication in school-age children (ages 6 to 14 years) who use AAC devices. Forty-two parents completed the survey which included background questions and two reliable questionnaires: the abbreviated Family Impact of Assistive Technology Scale for AAC and the Quebec User Satisfaction of Assistive Technology Scale.

**Results:** Parents were generally satisfied with their child’s AAC device and services. Children who were better at everyday communication were more independent and communicative with other people. This was not affected by the child’s age. Neither the places where children used their AAC device nor their success at school predicted their communication level. More research into AAC barriers and facilitators will help clinicians to plan ways to support children who need AAC.

### **A Randomized, Placebo-Controlled Study of Tideglusib in the Treatment of Adolescents with Autism Spectrum Disorder.**

Nicolson, R., Bennet, T., Thorpe, K., & Anagnostou, E.

**Objectives:** Autism Spectrum Disorder (ASD) is a common neurodevelopmental disorder that is characterized by social deficits and repetitive behaviours. No medications have been approved for the treatment of the core symptoms of ASD. Recent preclinical studies indicate that GSK3b is an enzyme that is overactive in key molecular pathways that are germane to neuronal functioning and neuronal plasticity in neurodevelopmental disorders. The purpose of this study was to assess the safety and efficacy of a GSK3b inhibitor in the treatment of adolescents with ASD.

**Methods:** The study used a 3-center Canadian clinical trial network. 83 adolescents between the ages of 12 and 18 years were randomized in a 1:1 double-blinded manner to tideglusib or placebo across a 12-week treatment period. For individuals blindly randomized to tideglusib, the dose was commenced at 400 mg each morning and then uptitrated to 1000 mg each morning. Outcome measures included caregiver- and clinician-completed rating scales.

**Results:** Tideglusib was generally safe and well tolerated, with adverse event rates that were generally similar between tideglusib and placebo. There were no treatment-associated serious adverse events. Most measures trended for greater improvement with tideglusib than placebo including measures of social withdrawal and repetitive behaviours. Statistically significant improvement was seen in overall adaptive functioning and social functioning.

**Conclusions:** In this trial, tideglusib was well-tolerated. Treatment with tideglusib resulted in significant improvements in functioning, suggesting that further study of tideglusib in patients with autism is warranted.

## Fatigue in Cerebral Palsy – Contributing Factors and Management Strategies

Brunton, L.

People with cerebral palsy (CP) experience significant fatigue that impacts many aspects of their daily lives. This study analyzed text responses from open-ended questions of the Fatigue Impact and Severity Self-Assessment to describe the factors that contribute to fatigue and the self-management practices used by youth and young adults with CP. The most commonly reported contributors to fatigue included: activity-related factors, general demands of life, sleep/rest, general health concerns, CP-related factors, mental health concerns and environmental factors. The top five strategies participants reported to manage fatigue included rest or relaxation, sleeping or napping, changing or limiting their activities, being physically active, or using specific adaptations or assistive devices. Results from this study suggest that there are potentially modifiable factors, including activity level and sleep, that significantly contribute to fatigue for persons with CP; these could form the basis of interventions targeted at the prevention and management of fatigue. A closer look at the impact of fatigue on participation in life events is warranted.

## Using Translational Behaviours to Study Sensory Processing in the *Cntnap2* Rat Model of ASD

Scott, K., Mann, R.S., Allman, B.L., & Schmid, S.

**Study Objectives:** The processing of sensory information is necessary for interactions with our environment; however, in individuals with autism spectrum disorders (ASD), impairments in lower-level sensory filtering may impact higher-order perceptions of complex sensory signals. Thus, this study aimed to establish a preclinical animal model with high face validity for ASD-related behavioural deficits to ultimately study the mechanisms underlying sensory behaviours in ASD.

**Methods:** Both sound intensity and multisensory processing at the pre-attentive and perceptual level were assessed in rats with a functional knockout of the *Cntnap2* gene. Pre-attentive processing was examined using the acoustic startle response and its modulation by a prior stimulus (i.e., prepulse). For cognitive testing, operant conditioning was used to assess the rats' ability to discriminate the relative sound intensity of noisebursts, or timing of auditory and visual stimuli.

**Results:** *Cntnap2*<sup>-/-</sup> rats exhibited a general impairment in prepulse inhibition, with no audiovisual prepulse integration deficit. Similar to autistic individuals, the *Cntnap2*<sup>-/-</sup> rats showed no deficits in perceiving the relative timing of simple auditory and visual stimuli compared to wildtypes. Moreover, despite *Cntnap2*<sup>-/-</sup> rats showing increased reflexive responses to moderately loud sounds, they had no difficulty in accurately discriminating sounds that varied in intensity.

**Conclusions:** Taken together, these results confirm that the reactive sensory processing impairments in ASD can be effectively studied in rat models using the aforementioned translational behavioural paradigms.

## Traumatic Life Events, Internalizing and Externalizing Symptoms in Children with IDD.

Lapshina, N., & Stewart, S.L.

**Background:** Children and youth with comorbid IDD and mental health diagnosis are more likely to experience verbal, physical, or sexual abuse, and to be bullied by age-mates, compared with children with IDD only (Taggart et al., 2010). However, there is limited research on poly-victimization in this population.

**Objectives:** To establish the prevalence and common patterns of poly-victimization among children with comorbid IDD and mental health problems. Additionally, we explored how poly-victimization patterns relate to internalizing and externalizing symptoms.

**Methods:** We utilized the interRAI ChYMH-DD database (N=657; 73.2% male; M age=11.88). Using frequency analyses, we estimated the prevalence of most common traumatic life events in this sample. Association tests and Generalized Linear modelling were utilized to examine relationships among variables.

**Results:** Experiences of bullying were the most prevalent form of trauma (21.6%), followed by witnessing domestic violence (WDV; 18.4%), emotional abuse (16.6%), parental abandonment (16.0%), physical abuse (14.8%), and other traumatic events. WDV was associated with being a victim of emotional, physical, and sexual abuse, and parental addiction. A domestic violence (DV trauma) variable was created to reflect polyvictimization; it included seven categories: no DV trauma, WDV only, emotional abuse only, WDV and emotional abuse, physical abuse only, emotional and physical abuse, and a combination of all three trauma types.

In GLM, controlling for gender and age, WDV only, emotional abuse only, WDV combined with emotional abuse, and a combination of all three trauma types predicted higher internalizing symptoms (vs. no DV trauma).

**Conclusion:** Despite some differences in predicting internalizing and externalizing symptoms from DV trauma, experiencing all three forms of DV trauma and emotional abuse predicted both internalizing and externalizing problems. These findings may inform service providers to design trauma-informed care and therefore prevent further complications in these children.

## Sensory Processing in ASD and ADHD: A Transdiagnostic Mechanism.

Schulz, S.E., & Stevenson, R.A.

**Objectives:** Sensory-processing issues are common in developmental disabilities, including autism (ASD) and attention-deficit/hyperactivity disorder (ADHD), and have been linked to clinical presentations. Here, we explored sensory processing, and its relationship with adaptive functioning, in ASD and ADHD.

**Methods:** Data were collected through the Province of Ontario Neurodevelopment Disorders Network from 519 participants with ASD, ADHD, or typical-development (TD), with the Childhood Behaviours Checklist (CBCL) assessing adaptive functioning and the Short Sensory Profile (SSP) assessing sensory processing.

**Results:** ASD and ADHD groups exhibited more severe sensory-processing and behavioural issues than the TD group. ASD displayed significantly fewer behavioural issues but presented with significantly greater sensory-processing issues than ADHD. The SSP was able to successfully predict diagnosis via a discriminant function analysis: 93% of TD participants were correctly classified, 63% of ASD participants, and 69% of ADHD participants.

In every group, sensory-processing issues predicted adaptive functioning. Models predicting adaptive functioning in ASD and ADHD did not significantly differ. Both were driven by Auditory Filtering and Underresponsiveness with the addition of Tactile Sensitivity in the ASD group. The TD model predicting adaptive functioning was driven by Auditory Filtering, Movement Sensitivity, and Visual/Auditory Sensitivity.

**Conclusions:** While the severity of sensory-processing issues differed across diagnostic groups, the manner with which sensory issues relate to behavioural outcomes appears to be quite similar between ASD and ADHD. Thus, while sensory processing can be used to discriminate between clinical and nonclinical participants, sensory processing may also act as a transdiagnostic mechanism that predicts outcome severity across diagnostic groups.

## Abstracts – Poster Presentations

### **Measuring the Meaningful: WHO's International Classification of Functioning, Disability, and Health (ICF) as a Tool to Analyze Measures for a Longitudinal Autism Study**

Nagee, A., Lakkadghatwala, R., Trinari, E., & Kraus de Camargo, O.

**Background:** The Pediatric Autism Research Cohort (PARC) project intends to develop a research protocol to be embedded in the Ron Joyce Children's Health Centre, McMaster Children's Hospital. Its purpose is to implement a process whereby the information provided by families in ASD service can be systematically utilized in research that will inform future treatment in the clinic. Measures used in the project were evaluated using the WHO's ICF classification to determine to what extent they encompass a child's functioning.

**Methods:** Using a process outlined by previous literature, two researchers independently linked each item in each measure to an ICF code then established consensus for discrepancies. A literature review of prior linkages to the same measures was then conducted and compared to our internal linkages. Three researchers then established consensus across all linkages, producing a final ICF code for each item.

**Results:** We provide an overview of the domains being assessed in the PARC study according to the ICF. Such information can be helpful in determining gaps and redundancies in selected measures. Linking measures to the ICF allows for greater comparability of study results obtained with diverse tools.

**Discussion:** Some measures selected had been linked previously utilizing slightly different methodology and we discuss the differences encountered. Some additional measures were linked to the ICF for the first time and this information is available for future studies. The results demonstrate the intended broad approach of going beyond symptom severity by collecting information about impacts on participation and influence of environmental factors.

### **Evaluation of a Social Support Program for Children with Down Syndrome and Their Typically Developing Siblings.**

Amicarelli, A., Miko, J., & Neil, N.

Siblings are a critical part of lifelong support for individuals with Down syndrome (DS). Children with DS demonstrate deficits in social, communication, and play skills resulting in atypical interactions with others, including siblings. Typically-developing (TD) siblings also face their own social-emotional adjustment needs. The needs of both the TD sibling and the child with DS may be addressed through programs with interventions for the social, communication, and play skills of children with DS and support groups specifically for the TD siblings. This study examined the effects of a 9-week social skills support program on the sibling relationship and the TD siblings' adjustment. Two sibling dyads completed the program consisting of skills instruction for children with DS, a support group for TD siblings, and cooperative recreation activities for all children together. Standardized questionnaires, direct observations, and qualitative analyses were used to measure the sibling relationship and typical siblings' adjustment. Results show preliminary evidence for the effectiveness of this social skills support program for children with DS and their TD siblings. Implications for future research and practice are outlined.

## **Brain Metabolite Dynamics in First-Episode Schizophrenia Using 7.0-Tesla Functional Magnetic Resonance Spectroscopy.**

Jeon, P., MacKinley, M., Dempster, K., Palaniyappan, L., & Theberge, J.

**Study Objectives:** Recent findings that glutamate N-methyl-D-Aspartate receptor antagonists are able to replicate the full range of schizophrenia symptoms show promise of glutamate research explaining the mechanisms behind schizophrenia symptoms. This research proposes dynamic glutamate measurements may be a more sensitive early marker in schizophrenia treatment outcome and aims to show abnormal glutamate dynamics in individuals with first-episode schizophrenia compared to healthy controls.

**Methods:** Glutamate dynamics were measured using a 7-Tesla proton functional magnetic resonance spectroscopy (fMRS) semi-LASER pulse sequence in the dorsal anterior cingulate cortex for 14 first-episode schizophrenia and 16 healthy control participants. The Stroop task performed during the fMRS data acquisition consisted of rest, active, and recovery periods.

**Results:** The mean Cramer-Rao Lower Bounds of glutamate level quantifications were  $3.23 \pm 0.99\%$  for healthy controls and  $3.41 \pm 0.81\%$  for first-episode subjects. Only a strong trend was observed toward increasing glutamate levels upon activation and decrease of glutamate levels upon removal of Stroop stimulus. We also noted that first-episode subjects had more reduced levels of glutamate during recovery periods.

**Conclusions:** Increasing sample size will help reduce variation within each period and is expected to contribute to seeing significance between each period of the fMRS paradigm. Results from this work will help develop approaches to identify patients who will experience poor outcome and/or treatment resistance early in the course of illness so that alternative to standard treatment algorithms can be considered. Stratification of patients entering a drug trial is another foreseeable application.

## **Supporting Treatment Plans for Children/Youth with Developmental Disabilities to Address Factors Associated with Caregiver Distress.**

McKnight, M., Theall, L., & Stewart, S.L.

**Study Objectives:** Consider challenges faced by caregivers of children and teens with developmental disabilities. While some caregivers cope well, others experience significant levels of stress. This study's objective was to examine the mental health characteristics of children/teens and family functioning of caregivers with high levels of distress.

**Methods:** A sample of 551 children/teens with developmental challenges (ages 4-18) were assessed using the interRAITM Child and Youth Mental Health and Developmental Disability tool (ChYMH-DD). Scales and Collaborative Action Plans (CAPs), developed in collaboration with international experts, are key features of the ChYMH-DD assessment. Scales indicate the degree of severity for issues. CAPs identify areas of need and provide evidence-informed guidelines for intervention. In this sample, 230 (42%) children/teens were flagged by the Caregiver Distress CAP as needing support for their caregiver struggling with excessive stressors. Dividing the sample into those flagged by the CAP and those not, six scales were analyzed for group differences: Disruptive/Aggressive Behaviour (DABS), Anxiety, Hyperactive/Distracton (HDS), Sleep Difficulties, and Family Functioning Scales.

**Results:** A one-way ANOVA indicated that caregivers with excessive stress have children/teens with more severe mental health challenges and are struggling with family dysfunction: DABS [ $F(1, 549) = 18.57, p < .001$ ], Anxiety [ $F(1, 549) = 8.34, p = .004$ ], Sleep Difficulties [ $F(1, 549) = 4.27, p = .039$ ], and Family Functioning [ $F(1, 549) = 199.13, p < .001$ ].

**Conclusions:** The results suggest that caregivers of children/teens with developmental challenges would benefit from services for their child/teen's mental health and supports to improve family functioning.

## **Family Dynamics, Trauma, and Child-Related Characteristics: Examining Factors Associated with Co-Morbidity in Children With and Without an Intellectual Development Disorder.**

Dave, H., Stewart, S., & Lapshina, N.

**Study Objectives:** Psychiatric disorders are common in children and youth with intellectual development disorder (IDD). This is a vulnerable group of children whose behavioural problems often have more complicated care needs than other children, which can place a great deal of stress on their families. However, the association of family functioning in this context is relatively under-studied. The purpose of the proposed study is to establish the relationship among family functioning factors, behaviour problems (particularly, self-injury and aggression), and disruption in care among children and youth with and without IDD.

**Method:** We used two samples of clinically-referred children and youth with (N = 657) and without (N = 9002) an IDD. Generalized linear models with robust estimation were used to assess the prediction of the following dependent variables: presence/absence of IDD, as well as co-morbidity in both samples.

**Results:** Our study found that children with IDD were more likely to be older, male, and have a history of exhibiting self-injurious behaviour. In addition, co-morbid psychiatric diagnosis was highly associated with several family functioning problems in both children with IDD and without IDD.

**Conclusions:** Overall, our study reveals that children with dysfunctional families tend to exhibit greater levels of comorbidity than those without familial dysfunction. Implications for care-planning are discussed.

## **Emotional Face Stimuli Evokes Regionally-Specific Activation in The Amygdala in Adolescents and Adults With Autism Spectrum Disorders.**

Sequin, D., Chen, J., Nicolson, R., Martinez-Trujillo, J., & Duerden, E.

**Objectives:** Using meta-analytic methods, to determine whether individuals with ASD demonstrate differential activation in brain regions involved in processing emotional face stimuli, compared to those who are typically developing (TD). We aim to examine whether task differences in gaze affect regional activation in the brain, particularly the amygdala.

**Methods:** A comprehensive literature search was conducted for studies which included comparisons of functional magnetic resonance imaging (fMRI) data acquired during an emotional face viewing task between individuals with ASD and TD controls. BrainMap GingerALE 2.3 was used to conduct an ALE meta-analysis.

**Results:** A total of 22 studies were identified. Analyses confirmed significant bilateral amygdala activation in both TD and ASD individuals. A measure of constrained gaze to the eye region of the stimuli was identified in 8 of these studies which were included in a sub-analysis examining effects of constrained gaze on the tasks. This sub-analysis revealed hyperactivation of the left amygdala in ASD individuals compared to TD controls ( $p < .001$ ).

**Conclusions:** ASD and TD participants employ different networks when processing emotional face stimuli. Results suggest individuals with ASD are experiencing increased arousal when viewing the eye region of emotional stimuli. Desire to avoid this negative response may underlie atypical gaze patterns in ASD individuals.

## Addressing the Question of Whether Statistical Learning Underlies Language and Reading Impairments.

Moreau, C., Child, I., Liesemer, K., Batterink, L., & Joanisse, M.

**Objectives:** Our ability to build our vocabulary simply through exposure relies on us becoming sensitive to structural patterns in the environment, a process known as statistical learning (SL). Impairments in SL result in the inability to detect structural patterns, which may underlie impairments in language and reading. Yet, research on SL in children with a broad range of language and reading abilities is largely unexplored. The goal of the study was to explore how SL predicts patterns of deficit in multiple language modalities to provide a more complete picture of how SL influences language and reading development. The hypothesis was that children who have poor language and reading profiles will also have poor SL abilities.

**Methods:** To test whether SL is related to language and reading abilities, we recruited children between 8 and 12 years and looked at their performance on an auditory and a visual SL task. In addition, we recorded event-related potentials during the exposure period of both SL tasks, which provided us with information on the nature and time course of learning. We tested 40 participants (M=10.1 years, range: 8.1-12.7 years) with a range of language and reading abilities, including children with language and reading impairments. The participants were English monolingual, with normal or corrected-to-normal vision, no history of hearing impairment, or other neurological disorders. Participants were given a battery of language and cognitive tasks to determine their reading and language proficiency. Children's brain activity was monitored with electroencephalogram while they completed auditory and visual SL tasks. For the auditory SL task, participants passively listened to a 6-minute artificial language composed of four trisyllabic nonsense words. Participants then completed memory tasks to assess implicit and explicit learning of the novel language. For the visual SL task, participants observed a successive stream of aliens on the computer screen for 4.5 minutes. Unknown to participants, the aliens were grouped into trios. SL was assessed with an explicit forced choice recognition task.

**Results:** The reading and language measures were not significantly correlated with auditory SL. However, phonological awareness was significantly correlated with performance on the visual SL task, suggesting that poor visual SL is related to poor phonological awareness. Impairments in phonological awareness could lead to problems in detecting and manipulating phonemes, which is linked to Reading Disability (also known as dyslexia) and Developmental Language Disorder (DLD; previously Specific Language Impairment). These findings partially support our hypothesis that poor SL underlies language and reading impairments. In addition, IQ was significantly correlated with implicit auditory SL, suggesting that SL may underlie nonverbal IQ.

**Conclusions:** These findings provide us with insights on the emergence of language and reading impairments. In addition, this research provides us with novel behavioural and neuroimaging data on the relationship between SL and language and reading.

## Neural Representations of Gaze Direction in Primate Basolateral Amygdala.

Mahmoudian, B., & Martinez-Trujillo, J.

**Study Objectives:** Introduction: Social communication in primates relies heavily on visual cues. Head and eye orientation can signal one's gaze direction, providing cues for directing attention. In the primate brain network proposed to support social cognition, the amygdala has been shown to respond to elements of a face such as eyes. Although amygdala lesions impair performance of individuals in spatial cueing tasks utilizing social cues (eye) there exists little evidence of how the local amygdala circuitry might encode gaze direction. To address this gap we have designed a spatial cueing task in which the animal must utilize gaze direction cues to locate the rewarded target while single unit activity of BLA is monitored.

Hypothesis: Different populations of neurons in primate BLA are tuned for gaze cues of head and eye orientation and the social valence of a stimulus is critical for amygdala's involvement in visual processing.

**Methods:** Two Rhesus Macaques will be placed in front of a computer screen while their eye positions on the screen are monitored and single neuron activity in the BLA amygdala is recorded. In a four-alternative choice task, the animal must utilize the presented direction of social or non-social cue to attend the location of the rewarded target. Social conditions include 3D virtual monkey models cueing the target location using different combinations of head and eye rotations. Non-social conditions will employ a variety of non-biological cues (e.g. an arrow).

**Results:** Correlating neural activity with presentation of social and non-social stimuli, we anticipate neurons in the BLA amygdala will be tuned for the direction of gaze and/or individual components of gaze (e.g., head orientation).

**Conclusions:** Results could have strong implications for the study of developmental disorders such as Autism Spectrum Disorder in which amygdala abnormalities are observed.

## The Effects of Adolescent Stress on Schizophrenia.

Dong, S., & Rajakumar, N.

**Study objective:** The etiology of schizophrenia can be understood through the "two-hit" model. The first "hit," or insult creates a predisposition by disrupting early neurodevelopment. This increases one's vulnerability to a second insult later in life, which may lead to schizophrenia manifestation. The second insult may occur at any time during development; however, adolescence merits attention as schizophrenia symptoms often manifest during and after this time. This study aimed to understand how psychological stress during adolescence affects schizophrenia manifestation when in the presence of a predisposition. We hypothesized that exposure to non-traumatic, mild psychological stressors during adolescence in the presence of a predisposition contributes to abnormalities that are reminiscent of schizophrenia.

**Methods:** Male and female Sprague-Dawley rats received bilateral injections of either nerve growth factor (NGF) or saline (control) into the developing medial prefrontal cortex. NGF-animal models have been previously established to be a putative model of schizophrenia. Rats were exposed to mild, non-traumatic psychological stressors during their adolescence (PND 26–40) and their behaviours were studied during adulthood (after PND 70).

**Results:** Observed trends showed that adolescent stress did not affect cognitive function and sensory gating in predisposed animals, while it showed opposite, sex-specific effects in wild-type animals. In addition, adolescent stress significantly enhanced dopamine sensitivity, but only in predisposed, female animals.

**Conclusion:** Adolescent stress influences schizophrenia manifestation in the presence of a predisposition, albeit through a sex-specific manner.

## Acoustic Startle Response in Children with Autism Spectrum Disorder with and without Co-Morbidity of Attention Deficit Hyperactivity Disorder.

Phillips, R., Schmid, S, & Nicolson, R.

**Background:** Parents of children with Autism Spectrum Disorder (ASD) and or Attention Deficit Hyperactivity Disorder (ADHD) often report that their children have trouble “tuning out” sensory stimuli. It is estimated that over 96% of children with ASD have difficulties filtering sensory information. Typically, no objective physiological measures of sensory filtering are assessed. Though many symptoms overlap between ASD and ADHD and some estimates of comorbidity are as high as 50%, there is evidence that the underlying causes of these conditions may differ. An objective method for assessing sensory filtering ability is to study the eye-blink component of the startle reflex (SR) in response to unexpected startling sounds. The subject’s ability to habituate to these random noises can be quantified and compared to traditional diagnostic tools.

**Objectives:** This study sought to quantify the differences and similarities in sensory filtering among individuals with ASD, ADHD, both ASD and ADHD (Dual), and those with neither ASD nor ADHD (Control). A second objective was to compare EMG SR data to current clinical measures of sensory-related behaviours.

**Methods:** Data from 32 participants aged 9-17 years were grouped according to diagnostic status into one of the four groups mentioned above. All individuals were assessed using pencil and paper standardized tests for characteristics of ASD and ADHD, their Sensory Profiles, as well as the Raven’s Progressive Matrices as a measure of non-verbal intelligence. Orbicularis oculi electromyography (EMG) measurements were recorded during an acoustic startle protocol that included input/output function, and habituation. Baseline EMG, SR amplitude, and response latency were compared between groups. Welch’s Anova and Games-Howell post-hoc analysis was conducted to determine statistical significance of findings.

**Results:** Baseline average EMG voltage of participants with ADHD was significantly higher than that of baseline voltage for any other group. The Control group’s average amplitude of startle response was significantly lower than any other group. ADHD and Control Groups had similar SR latency and were both significantly faster than that of both ASD and the Dual group. Baseline, SR amplitude and SR latency was not strongly correlated to any parent reports, IQ or age. Parent-reported characteristics of ADHD strongly correlated to the Sensory Profile but not to ASD characteristics.

**Conclusions:** The results of this work demonstrate that there are differences between the population of individuals who have ASD with ADHD and those that have ASD without ADHD. The correspondence of the EMG data to subjective measures indicates limitations in relying on third-party subjective assessments for diagnostic purposes. The EMG SR of the groups will inform the validity of animal models of autism currently being used in basic research and further develop the neuroscience models of sensory filtering pathways.

## **Fruits of Genomic Match-Making: De Novo Variants in PRR12 are Associated with a Wide Spectrum of Eye and Neurodevelopmental Anomalies.**

Balci, T.B., Wang, L., Lalani, S., Heide, S., Keren, B., Mignot, C., Morley, G., Walia, J., Wheeler, P., Lemons, J., Rodriguez-Buritica, D., Riberi, E., Biamino, E., Schatz, K., Gunay-Aygun, M., Wiesener, A., Zweier, C., Wentzensen, I., Siu, V.M., & Bi, W.

Rare disease research has made great strides in the last decade; first with unbiased genome-wide sequencing methods, then with global data-sharing efforts. Genomic match-making has accelerated the path from candidate gene identification to establishing causality. Identification of multiple unrelated individuals with variants in the same gene followed by “reverse phenotyping” has become the mainstay of next generation syndrome delineation.

Using exome sequencing, we identified a de novo frameshift variant in the PRR12 gene in a 2-year-old girl with anophthalmia and developmental delay. PRR12 is highly expressed in the brain and the visual system. It has a high missense constraint score ( $Z=3.37$ ) and no loss of function variants listed in gnomAD ( $pLI=1.00$ ). De novo truncating variants in PRR12 were recently reported in three individuals with developmental delay and iris abnormalities. Through GeneMatcher, we were connected to 11 additional patients from around the globe with de novo PRR12 variants. There was one recurrent variant; all but one, were truncating; and none were listed in gnomAD at the time of abstract submission. A variety of eye abnormalities were observed in 7/12 individuals; including severe myopia, stellate iris, coloboma, Rieger’s anomaly, microphthalmia, cryptophthalmos and anophthalmia. Developmental delay was noted in 10/12 individuals, two of whom had severe intellectual disability. There were growth delays in several individuals (3 with short stature and 3 with microcephaly).

The overlapping clinical findings, especially the ophthalmological features, support an association between haploinsufficiency of PRR12 and a distinct neurodevelopmental disorder. At this time, features are variable and functional data is needed to confirm pathogenicity. We plan to use zebrafish and mouse models to replicate the eye and growth phenotypes and further investigate the pathogenicity of different PRR12 variants. This cohort once again demonstrates the benefits of global data sharing efforts in novel gene discovery.

## **Training in Developmental Disabilities in Canadian Psychiatry Residency Programs: Residents Perspectives.**

O’Flanagan, S., Hallock, S., & Nicolson, R.

**Objectives:** Research indicates that rates of Psychiatric Disorders are very high in people with Developmental Disabilities (DD). However, research also suggests that teaching devoted to Developmental Disabilities in Psychiatry Residency Programs in Canada varies significantly in regards to both didactic teaching and supervised clinical rotations. Very little research has examined training in ID from the perspective of psychiatry residents. The purpose of this study is to determine how senior residents perceive their educational experience in regards to developmental disabilities.

**Methods:** A survey regarding training in developmental disabilities was distributed to senior residents at an exam review course in the final 6 months of their training.

**Results:** 91.5% of respondents reported receiving some lectures or seminars on DD during their residency training. 46.8% of respondents reported that their program required them to complete a rotation in DD, though the length of the rotation, the stage in the lifespan specific to the rotation, and the year in which the rotation was completed varied significantly. 91.5% of respondents also reported that their level of comfort in assessing and treating psychiatric disorders in people with DD was very low.

**Discussion/Conclusion:** Senior residents report significantly different training experiences in DD, although overall experience with this population is low for most residents. This has an impact on levels of confidence in treating this population, and potentially the quality of care for people with developmental disabilities.

## **Violence Against Women with Intellectual Disabilities in Canada: A Systematic Review.**

O'Flanagan, S., Boldt, G., & Nicolson, R.

**Background:** The government of Canada reports that 1 in 3 Canadian women will be the victims of sexual assault or Intimate Partner Violence (IPV) in their lifetime. Women with Intellectual Disabilities are reported to be the victims of sexual assault or IPV 7 to 8 times more than the typically developed population.

**Objectives:** The objective of this review was to investigate prevalence rates of sexual assault and IPV against adult women with Intellectual Disabilities (ID) in Canada, and to examine reasons behind the increased rates of violence against this population.

**Methods:** This systematic literature review was guided by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA). A search of multiple electronic databases was conducted (e.g., PubMed, PsycINFO, MEDLINE, OVID, CINAHL, Gender Studies Database, COCHRANE, SCOPUS, Web of Science, etc.) and manual searches of journals (e.g., Canadian Journal of Disability Studies) were used to locate articles written in English and published in peer-reviewed journals up to the present. The search strategy included terms for violence, disability and Canada. Articles included met the following criteria: 1) Specific to Canada, 2) focused exclusively on, or included data specific to women with ID.

**Results:** The search yielded 2,948 record hits and the full text of 26 articles were screened. After full text screening, 11 articles met all criteria. All excluded articles were either not specific to Canada, or focused only on physical disability.

**Conclusions and Implications:** The findings from this systematic literature review indicate that women in Canada with ID are at a higher risk of being the victims of sexual assault or IPV than women in Canada with no disability, and then men with ID. The findings also indicate that women with ID face multiple barriers to reporting violence to authorities that women with no disability do not face. It also indicates that these women are the victims of violence more often than the other two groups previously mentioned because of the intersection of sexism and ableism.

## **Neurodevelopmental Outcomes in Infantile Hydrocephalus: An fMRI Case Study.**

Ahmed Hashi, I., de Ribaupierre, S., & Eagleson, R.

Ventricle dilatation, caused by infantile hydrocephalus, can lead to compression of surrounding cortical regions, which may result in an assortment of mental and physical impairments. Due to the posterior to anterior progression of infantile hydrocephalus, posterior brain regions, such as the parietal and occipital cortices, will undergo the worst extent of damage. We postulate that damage of the posterior cortex caused by ventricular dilatation in infantile hydrocephalus will lead to nonverbal learning deficits, seen in school-aged children. This case study will focus on three hydrocephalus patients who were shunted within the first two years of life. We examined the functional outputs of the posterior cortex, which primarily regulates non-verbal cognition, specifically numeracy, shape recognition, and visuospatial skills, through task-based fMRI as well as normative behavioural assessments. Cluster-based fMRI analysis was used to determine brain activation during a comparison task of numbers, faces and shapes. During the number condition bilateral intraparietal sulcus and superior parietal lobule activation was localized for both the healthy control group and individual hydrocephalus patients. Hydrocephalus patients displayed general trends of lower scaled scores in non-verbal assessments of various behavioural tests (Beery VMI, WISC, and WPPSI). Hydrocephalus patient performance of shape assessments (Beery VMI, and Visual Perception) was correlated to percent signal change during the shape condition in the right inferior parietal lobule. The findings as well as the methodology of this case study will offers new possibilities for future research using task-based fMRI a measure of pathological changes to brain functional anatomy in pediatric neurological conditions such as hydrocephalus.

## Quality of My Life and Fatigue: Perceptions of Boys with Duchenne Muscular Dystrophy and Their Caregivers.

Bhullar, G., Wei, Y., El-Aloul, B., Speechley, K., Miller, M.R., & Campbell, C.

**Background:** As there is no cure for Duchenne muscular dystrophy (DMD), current management aims to improve quality of life (QoL). DMD studies that use measures of QoL and health-related quality of life (HRQoL) recognize them as separate constructs; however, investigations of factors associated with either or both constructs are limited. Fatigue has been shown to be the strongest predictor of poor HRQoL in boys with DMD using a multi-dimensional a HRQoL measure. Our objective was to examine the association of fatigue with single-item QoL and HRQoL profiles in a DMD population.

**Methods:** Participants (N=211 children and/or parents) identified via the Canadian Neuromuscular Disease Registry completed the Quality of My Life (QoML) questionnaire which includes a QoL Visual Analog Scale (VAS) and a HRQoL VAS. Higher scores (max=10) reflect better QoL and HRQoL. Fatigue was assessed using the PedsQL Inventory™ Multidimensional Fatigue Scale (MFS), with higher scores (max=100) reflecting less fatigue. Descriptive statistics were computed and ANOVA or linear regression analyses assessed the association of fatigue with both child self-reported and parent-reported QoL and HRQoL controlling for clinical and family characteristics.

**Results:** Mean(SD) QoL and HRQoL scores were 7.76(1.89) and 7.34(2.18) for child-reports and 7.05(1.99) and 6.99(1.97) for parent-reports, respectively. Mean (SD) MFS scores for child- and parent-reports were 71.12(16.15) and 68.98(18.00), respectively. Fatigue was positively associated with both QoL and HRQoL for child-reports [B(SE)=0.04 (0.01), p=0.004, R<sup>2</sup>=0.16; B(SE)=0.03(0.01), p=0.021, R<sup>2</sup>=0.13] and for parent-reports [B(SE)=0.03(0.01), p=0.013, R<sup>2</sup>=0.18; B(SE)=0.03(0.01), p=0.005, R<sup>2</sup>=0.12].

**Conclusion:** Fatigue predicts worse QoL and HRQoL for boys with DMD by both child self- and parent proxy-report. Therapeutic strategies aimed at reducing fatigue may therefore improve QoL and HRQoL.

## Health-Related Quality of Life and Fatigue in Children with Duchenne Muscular Dystrophy: A Three-Year Longitudinal Study.

Bhullar, G., Wei, Y., El-Aloul, B., Speechley, K., Miller, M.R., & Campbell, C.

**Background:** Longitudinal data on health-related quality of life (HRQoL) and fatigue in paediatric Duchenne muscular dystrophy (DMD) are limited. Recently, fatigue was reported to be the greatest predictor of poor HRQoL in paediatric DMD. Understanding the trajectory of HRQoL and its relationship with fatigue may facilitate the development of improved therapeutic strategies. Our objective was to describe three-year changes in HRQoL and fatigue in children with DMD.

**Methods:** Patients 4 to 17 years of age identified via the Canadian Neuromuscular Disease Registry received mailed questionnaires between 2013 and 2016. HRQoL was assessed using the Pediatric Quality of Life Inventory™ (PedsQL™) General Core Scales (GCS) and Neuromuscular Module (NMM), and fatigue was assessed using the PedsQL™ Multidimensional Fatigue Scale (MFS) by patient and parent report. Mean three-year change (Time 3 - Time 1) in scores were computed. Pearson correlations were computed between three-year change in HRQoL and fatigue.

**Results:** Mean decline in MFS scores for patient- and parent-reports were 1.03 and 1.19, respectively. Mean decline in GCS scores for patient- and parent-report were 1.75 and 4.13, respectively. Mean change in NMM scores for patient- and parent-report were 0.72 and -8.36, respectively. Change in MFS score was associated with changes in GCS ( $r=0.72$ ,  $p<0.001$ ) and NMM scores ( $r=0.84$ ,  $p<0.001$ ) by patient-report.

**Conclusions:** Children with DMD experience worse fatigue and HRQoL over time. Parents perceive a greater decline in HRQoL over time compared to patients.

## **The Relationship Between Emotion Recognition Ability, Subjective Emotional Intensity, and Traits Associated with ASD.**

Shafai, F., Gateman, E., Stow, M., Montenegro, J., Abraham, A., & Stevenson, R.A.

Autism Spectrum Disorder (ASD) is a developmental disorder that impacts the individual throughout the lifespan. Traits associated with ASD are found in the general population. Previous research has found that the ability to recognize emotions is impaired in autistic individuals. Additionally, eye-tracking data has indicated abnormal pupillary responses when viewing emotional stimuli. In this study of 100 neurotypical individuals, participants were asked to view videos of actors saying the same phrase while expressing different emotions. Actors expressed anger, disgust, fear, happiness, sadness, surprise at high and low intensities, in addition to a single neutral condition. Participants were asked to indicate which emotion they had just observed and then to subjectively rate the intensity of the emotion. Eye-tracking data was collected during the experiment and pupillary responses were analyzed to determine which emotions elicited the largest changes compared to the neutral condition. Participants were also asked to complete questionnaires assessing traits commonly associated with ASD. Results from the eye-tracking experiment were compared to the questionnaire data to see if there were any significant associations between pupillary responses, emotion recognition accuracies, subjective intensity ratings, and traits associated with ASD. Preliminary analyses indicate that emotion recognition accuracy was negatively correlated with the social knowledge subscale of the Multidimensional Social Competence Scale (MSCS) for disgust and sad emotions. Subjective emotion intensity ratings were negatively associated with the social motivation subscale of the MSCS for both high and low intensities of anger, fear, and sad emotions. Pupillary responses were negatively correlated with the social motivation subscale of the MSCS for anger and the social inferencing for sad emotions (all  $p$ -values  $< 0.05$ ). These results indicate that the ability to accurately recognize emotions, subjective ratings of the emotional intensity, and physiological pupillary responses when observing emotions are negatively associated with social competence.

## **Does Ventricular Volume Affect the Neurodevelopmental Outcome in Infants with Intraventricular Hemorrhage?**

Lo, M., Kishimoto, J., Eagleson, R., Bhattacharya, S., & de Ribaupierre, S.

The objective of this study was to investigate whether ventricular volume in infants with post hemorrhagic ventricle dilatation impacts neurodevelopmental outcome. Forty-nine infants who suffered an intraventricular hemorrhage in the neonatal intensive care unit at Victoria Hospital were enrolled in the study. Infants were scanned multiple times with 3D cranial ultrasound during their clinical course, and images were semi-automatically segmented to measure the total volume of the lateral ventricles, with the highest volume ever recorded used for analysis. Infants with a volume  $\leq 20$ cc were considered low-volume ( $n=33$ ), and infants with a volume  $\geq 40$ cc were considered high-volume ( $n=12$ ). Infants with a volume between 20cc and 40cc were excluded from the analysis ( $n=4$ ). Developmental outcome was assessed at 4, 8, and 12 months corrected age (CA) with the Alberta Infant Motor Scale (AIMS) and Infant Neurological International Battery (Infanib), and at 24 months CA with the Bayley Scales of Infant Development 3e (BSID III). Infants in the low-volume group had higher scores on the Infanib at 4 months CA, and on both the AIMS and Infanib at 8 and 12 months CA, even after controlling for gestational age, birth weight, and worst grade of IVH. Low-volume infants also scored higher on the cognitive and gross-motor subtests of the BSID III at 24 months CA. The results of this study show that ventricular volume affects neurodevelopmental outcome in infants with IVH. This finding could guide the timing of future interventions, as earlier intervention may decrease the likelihood of adverse neurodevelopmental outcome.

## **Analyzing the Electrophysiological Effects of Rett Syndrome on Neuronal Network Development Using Machine Learning.**

Khaki, M., Pradeepan, K., & Martinez-Trujillo, J.

Rett Syndrome is a genetic neurodevelopmental disorder caused by an MECP2 mutation that results in deficits characteristic of classical autism spectrum disorder. Multielectrode array technology is capable of measuring different aspects of electrophysiological features of the developing neuronal network. However, the amount of data produced is too large to manually explore and extract meaningful patterns. Using a machine learning technique allows us to reduce the amount of redundant information captured during the experiment. Using a supervised classification approach, it is possible to reveal the characteristic differences between normal and Rett syndrome affected cells. Although the higher volume of information encapsulates the different aspects of the problem it also leads to significantly increased observations and exacerbates the computational complexity. The preliminary results generated by the approach demonstrates that it is possible to rescale the solution to include sufficient number of observations. The results of the pilot experiment show that the differences can be categorized into three distinct developmental periods (early, intermediate, late). These inconsistencies indicate that the rate of growth for Rett syndrome is significantly stunted compared to wildtype, consistent with previous literature. This confirms that the relevant features extracted and selected in classification are biologically meaningful in distinguishing Rett syndrome.

## **Modeling Executive Functioning Development in Chinese and Canadian Children: A Novel Mobile Assessment Game Battery Approach.**

Pham, J., Goldsmith, S., Hampshire, A., & Morton, J.B.

**Background:** Executive functioning (EF) is a collective construct, encapsulating a set of higher-order cognitive abilities involved in goal-directed functions and behaviours. Of particular interest are response inhibition, working memory, and planning/organization executive processes. Developing standardized psychometric instruments that measure normal childhood EF development are crucial for identifying early onset cognitive deficits. However, task batteries such as the Developmental Neuropsychological Assessment (NEPSY) and Cambridge Neuropsychological Test Automated Battery (CANTAB) predominantly measure multiple cognitive domains in adults rather than in children.

**Objective:** Validation and optimization of the Mobile Assessment of Executive Functioning (MAXFun) game battery as a novel psychometric instrument that will improve on global mobility, data security, privacy, and presentation towards children.

**Method:** The Behaviour Rating Inventory of Executive Functioning (BRIEF-2) questionnaire will be used as a standardized validation measure of observed EF performance to compare against scores on the MAXFun battery. Approximately 115 children from primary schools in Shanghai, China, from 8 to 12 years old, with typical EF performance have participated in a preliminary validation study. Exploratory factor analysis (EFA) will be performed on preliminary data to determine which games in the battery accurately measure EF processes. Post-validation analyses, games with low validity will be adjusted for difficulty or timing of stimuli presentation. Once the battery has been optimized, a pilot study in London, Ontario will be conducted to assess validity again in a confirmatory factor analysis (CFA).

**Conclusion:** The MAXFun game battery has significant value as a cross-cultural psychometric instrument that is researcher, clinician, and family-friendly.

## Maturation of the Amygdala Subnuclei in children with Neurodevelopmental Disorders

Chen, J., Seguin, D., Nicolson, R., Martinez-Trujillo, J., & Duerden, E.

**Background:** The amygdala, comprised of 13 subnuclei, centrally processes fear, emotion, and social behaviours. In typical development, the amygdala outpaces the cortex in terms of its early macrostructural growth. The accelerated growth of the amygdala reflects ability to adapt in response to dynamic environmental changes. Dysregulated amygdala cellular development may lead to a torrent of maladaptive neurodevelopmental events that affect the maturation of the amygdala, particularly the basolateral nucleus, the main receiver of sensory information. Examining the underlying neurobiology of the sustained growth of the amygdala is critical to determine when these processes deviate in disorders such as autism spectrum disorder (ASD) and other neurodevelopmental disorders including attention deficit hyperactivity disorder (ADHD) and obsessive compulsive disorder (OCD).<sup>1,2</sup>

**Objectives:** In a cohort of children with and without neurodevelopmental disorders to assess the macrostructural development of the amygdala subnuclei.

**Design/Methods:** A prospective cohort of 233 children (172 boys [74%], median age=10 years, IQR=8-13) were scanned with 3T MRI scanners at 3 sites using a standardized protocol including a volumetric T1 weighted sequence to quantify amygdala volumes. Amygdala subnuclei volumes were measured using Freesurfer. Generalized Linear Models were used to determine the association among the macrostructural development of the subnuclei in children with ASD, children with ADHD, children with OCD and typically-developing children, adjusting for biological sex, age and total cerebral volumes.

**Results:** The sample included children with ASD (n=111, 48%), children with ADHD (n=38, 16%), OCD (n=27, 12%) and (n=57, 24%). Bilateral basolateral nuclei were significantly larger in children with ASD, ADHD and OCD relative to typically developing controls. Additionally, the paralaminar nuclei and corticoamygdaloid transition zone ( $p < .001$ ) demonstrated significant group differences. No group differences were evident for the medial, central or cortical, nuclei (all,  $p > .05$ ).

**Conclusions:** Children with neurodevelopmental disorders demonstrated larger basolateral amygdala volumes, potentially reflecting maladaptive reorganization of this key brain region. The larger volumes seen in children with ASD, ADHD and OCD relative to typically-developing children may occur through postnatal disruptions in dendritic arborization, synaptogenesis, gliogenesis, neuronal migration or a combination of these factors. Improved understanding of the developmental trajectories of the amygdala subnuclei may provide insight into maturational disturbances underlying the behavioural pathology in children with neurodevelopmental disorders.

**Funding:** Province of Ontario Neurodevelopmental Disorders Network (POND), Ontario Brain Institute, Compute Canada

## **Epilepsy Worry in Adolescents and Young Adults with Childhood-Onset Epilepsy: An Exploration Ten Years After Diagnosis.**

Huang, C.W., Anderson, K.K., Zou, G., & Speechley, K.N.

**Purpose:** The unpredictable nature of seizures in epilepsy may provoke “epilepsy worry”—an apprehensive expectation of future seizures and their consequences. This research sought to describe epilepsy worry in adolescents and young adults (AYAs) with childhood-onset epilepsy ten years after diagnosis and their parents’ worries about their child’s health, and to examine the associations of epilepsy worry with depression and anxiety, which are prevalent co-morbid conditions in AYAs with epilepsy.

**Methods:** Data were from the Health-Related Quality of Life in Children with Epilepsy Study (HERQULES), a multicenter prospective cohort study that followed children with newly-diagnosed epilepsy for approximately ten years after diagnosis. Epilepsy worry was measured using items from the Quality of Life in Epilepsy (QOLIE) Inventory in AYA’s self-report.

**Results:** At the 10-year follow-up, 131 AYAs (mean age = 18) returned completed questionnaires. The majority (59%) of AYAs had achieved  $\geq 5$  years of seizure remission and 28% were currently taking anti-epileptic drugs. While the majority of AYAs had not experienced epilepsy worry in the past four weeks, 35% had experienced at least a bit of worry regarding having another seizure and 22% had at least a bit of worry regarding injuries from seizure within the past four weeks. Multiple linear regression analyses are underway to explore the relationship between epilepsy worry level and depressive and anxiety symptoms.

**Implications:** This research explores the characteristics of AYAs experiencing epilepsy worry and could highlight epilepsy worry as a distinct area of counselling for improving the emotional well-being in AYAs with childhood-onset epilepsy.

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