University of Washington

Winter 2016

RABLAB NEWSLETTER

GREETINGS FROM RABLAB!

HTTP://DEPTS.WASHINGTON.EDU/RABLAB/

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New Studies!

TWIN-2:

We are looking for identical twin pairs ages 4 and up in which at least one twin has Autism Spectrum Disorder (ASD) to participate in a genetic study. Participation includes delivery of saliva and blood samples, and answering questionnaires. In person visits to our lab are not required for participation!

SFARI SPARK:

The goal of the SPARK project is to collect genetic information on 50,000 individuals across the country with ASD and their families. Anyone with a diagnosis of autism can participate! Participation includes online registration and the delivery of a saliva sample. These samples will be analyzed for ASD-related genetic events. Families may choose to have their genetic testing results sent to a provider of their choice, should a genetic event related to ASD be found.

ABC-CT:

The ABC-CT study is a multi-site study focused on identifying potential biomarkers to better track social development in ASD for use in future clinical trials. This study will use measures like EEG, eye and video movement tracking, as well as spoken language tracking, to better understand social communication behaviors among individuals with and without ASD. We will be launching our main study in the spring and we are looking for children between the ages of 4-11 with and without ASD diagnoses.

Ongoing Studies!

GABA

We have seen 12 families so far! We are still looking for adults with and without ASD ages 18-30 to participate in a study of how the brain processes sensory information.

TIGER

We have seen 50 families so far! We are still looking for individuals ages 4 and up for a comprehensive study of particular genetic events associated with ASD.

ZEBRA

We have seen 60 families so far! We are still looking for families with children ages 8-17 for an EEG study of brain mechanisms and behavior in ASD.

If you are interested in participating in any of our studies, please contact us at (206) 616-2889 or rablab@uw.edu.

RABLAB is named after our principal investigator, Dr. Raphael A. Bernier. The Bernier Lab is committed to understanding the biological underpinnings of autism spectrum disorders (ASD) and other related developmental disabilities. We use a "genetics-first approach" by identifying rare genetic variants that are likely contributing to ASD and following up with an in-depth and multi-faceted evaluation to understand the individual and the family on many levels. Following this methodology, we seek to identify meaningful subtypes of ASD that have distinct etiologies and phenotypic presentations in order to lead to more individualized treatments and knowledge about outcomes for people and families with ASD.

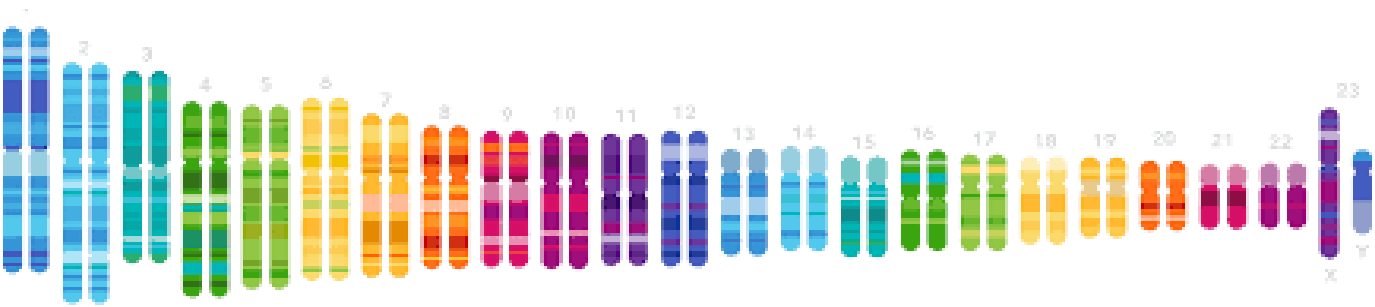
Lab Member Spotlight: Rachel Earl

Rachel Earl is a fourth-year doctoral student in the Bernier Lab. She is passionate about the diagnosis and treatment of autism spectrum disorders. When families come in for their visit, Rachel is one of the clinicians that does behavioral testing and interviews with children and parents. She loves meeting new families and learning about their experiences navigating medical, clinical and school services. When not with the Bernier Lab, Rachel loves hiking and cooking with her husband.

Rachel is studying the genetic impact of de novo likely gene disrupting (LGD) mutations on a child's behavioral functioning, such as cognition, language, and social interaction. De novo mutations arise anew in the child, and are not inherited from their parents. Thanks to your participation in our studies, we have been able to detect clear patterns of similarity between individuals with same LGD mutation. However, there continues to be some variability in the behavioral presentation of individuals with the same mutation.

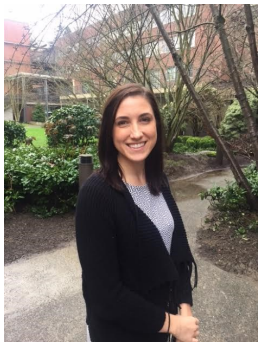
Traditionally, behavioral measures of a child's performance on tests of cognitive ability, language and social interaction are compared to a wide range of children their same age completing the same tasks across the country. When studying the impact that a de novo LGD mutation might have on a child's functioning, researchers have suggested that the extent to which a child's performance differs from their parent's performance in these same areas may be a better way to measure how a mutation impacts ability and behavior (see Moreno-de-Luca summary). In the general population, the cognitive functioning, language abilities, and social skills of most children have been shown to be similar to their parents. Understanding the difference between the performance of a parent and child when the child has a disruptive gene mutation may reveal where and how much a mutation is impacting a child's behavior. Looking first at parent-child differences in social responsiveness (as measured by questionnaire) for individuals with CHD8 disruptive mutations and CHD8-regulated target genes, Rachel found that difference scores are significantly larger for CHD8 than other LGD mutations and those with no disruptive mutation. This preliminary finding has implications for understanding the impact of CHD8-related genes on behavior.

Moreno-DeLuca et. al, 2015: In a recent publication, Moreno-de-Luca and colleagues looked at the genetic impact of de novo deletion on chromosome 16p11.2 (deletion of a piece of DNA arising anew, not inherited) on child outcome. Due to the heritability of traits such as cognitive ability, behavior, motor skills, and growth, the authors proposed using unaffected parent's performance as the measure of a child's expected outcome and comparing expected to observed child performance in order to to quantify the effect of 16p11.2 deletion on child outcome. Measures of cognition, behavior and motor skills of 56 children with a de novo 16p11.2 deletion were compared to that of their unaffected parents and siblings. In all areas, children with 16p11.2 deletion were more impaired than their unaffected parents and siblings. Relative to their parents, children with the deletion showed 1.7 standard deviation (SD) decrease in cognitive ability, 2.2 SD decrease in social behavior, and 1.3 SD decrease in motor performance. When compared to unaffected siblings, affected children showed 1 SD increase in body mass index. Significant correlations were found between unaffected parent (or sibling) and affected child in all measured areas, indicating that the observed outcome of children with 16p11.2 deletion is still tied to familial traits. In their proposed model, parental scores serve as a starting point for expected outcome and are adjusted for genetic impact to explain observed outcome for an affected child and the resulting variability between affected children. This work has important implications for thinking about trait variability amongst individuals with the same gene mutation and highlights the importance of considering familial background.



Mindfulness and Parenting

By Tracey Ward



Mindfulness is the awareness that arises by "paying attention in a particular way, on purpose, in the present moment, non-judgmentally." Mindfulness meditation is considered the heart of Buddhist practice, dating back to the 5th century B.C. Within the last 30 years, mindfulness practice called mindfulness based stress reduction (MBSR) has been used in fields of medicine, behavioral science, and neuroscience. During this influx of MBSR research, some scientists wanted to investigate whether parents of children with autism spectrum disorder (ASD) responded well to mindfulness as a method of stress reduction. Research suggests that parenting stress is four times greater for parents of children with ASD than parents of children with typical development and two times greater than parents of children with disabilities. The results found MBSR reduced parenting stress and symptoms of anxiety and depression, and improved sleep, well-being, and life satisfaction. One reason why mindfulness may be helpful in alleviating stress and improving well-being is the practice of physiological relaxation and the focus of a calm and present focused mind. For example, mindfulness emphasizes calming the body, such as using deep breathing or body scan techniques, while also encouraging one to do so nonjudgmentally and with compassion. Researchers theorize these practices act to "turn down" the automatic reactions and allow one to perceive situations as neutral . As a result, mindfulness emphasizes less avoidant coping and more active coping, less ruminative thought patterns and more acceptance, and less negative thinking styles and more positive reinterpretation of events. In doing this over time, perceptions and responses to stressful situations change in an enduring way. Below are some simple ways to practice mindfulness individually and incorporate mindfulness into parenting.

- **Mindful breathing:** you can sit or lay comfortably. Dedicate 5 – 10 min. per day and listen and focus on your breathing. If your mind wanders, simply notice and bring your attention back to your breath.
  - ***In a rush:*** When you're at a traffic light, focus on your breathing and count the number of breaths you take before the light changes.
  - ***Mindful Parenting:*** When your child is upset and they are offered a hug, embrace them and take three deep breaths along with them during the hug.
- **Mindful Listening:** This practice teaches us how to pay attention. Take one minute to be completely silent and listen to the sounds around you.
  - ***Mindful Parenting:*** You can do this with your child and ask them what they heard.
- **Gratitude:** Our brains are more sensitive to negative experiences than positive ones. When we can intentionally pay attention to positive things in our life, we strengthen the positive pathways in our brain. Make an intention to practice gratitude in your life daily.
  - ***In a rush:*** Keep a gratitude journal: each night write three to five things that you are thankful for
  - ***Mindful Parenting:*** When your children come home from school, instead of asking, "how was your day?" ask, "who was your friend today?"

Recent Lab Publications

We recently published (Hudac et al., 2015, Journal of Neurodevelopmental Disorders) results from our "genetics-first" work with the Simons Variation in Individuals Project (SVIP). The purpose behind this approach is to target individuals that have specific gene copy number variants (CNV, i.e., more or less copies of certain areas of DNA) or or single genes that are associated with the features of autism. Individuals with 16p11.2 deletions or duplications are likely to have neurodevelopmental issues, including language delay, behavioral problems, and autism. In our study, we wanted to learn about how the brain responds to social information in children and adults with 16p11.2 CNVs and how this compared to children with autism who do not have a known genetic variant. Participants watched videos of hands clapping (social motion) and tubes swinging (nonbiological, nonsocial motion) while we recorded brain waves using electroencephalography (EEG). We discovered that individuals with 16p11.2 CNVs have a unique social brain profile, such that their brains respond more strongly to nonsocial than social motion. This was different than individuals with autism (similar response for social and nonsocial motion) and typically developing individuals (stronger response for social motion). Interestingly, individuals with 16p11.2 duplications, whom often have less severe autism features compared to 16p11.2 deletions, do not differ from typically developing individuals until part-way through the experiment. In other words, at first, there is no difference between the groups, but eventually the brain response diverges from typical development for the 16p11.2 duplication individuals. Our findings strongly support the notion that children and adults with 16p11.2 CNVs exhibit atypical social brain responses, similar to, yet distinct from, autism. These results describe how individuals with 16p11.2 CNV respond to social information, critical for successfully navigating social interactions.