Center for Neurodevelopmental and Imaging Research at Kennedy Krieger Institute

Research Update – 2021

Dear Families,

I hope that you have all been able to sustain good health and spirits under the challenging circumstances of the past year. We recognize that the impact of the ongoing crisis has been profound for children and their families. These past months have allowed us to reflect on the substantial contributions that you make to our research efforts at the Center for Neurodevelopmental and Imaging Research (CNIR), and how these efforts can best help improve the lives of children and their families.

The CNIR remains dedicated to better understanding the behaviors and brain circuits involved in neurodevelopmental disorders like attention-deficit/hyperactivity disorder (ADHD), autism spectrum disorder (ASD) and Tourette syndrome (TS). The goal of this work is to improve how we care for, and intervene to help, children facing these challenges. For instance, in a recently published study, we reported on the benefits of a mindful movement (tai chi) practice for children with ADHD. We greatly appreciate all of your efforts in helping us make progress toward these goals. Without dedicated families like yours, we would not be able to gather the information needed to make progress in our research.

In terms of how the crisis has affected our work at the CNIR, while in-person testing has been halted since the beginning of the pandemic, we were able to transition some aspects of our studies to remote assessments last year. This past spring, we resumed in-person testing, making sure to take all necessary precautions for the safety and well-being of participating children and families, which always remains our top priority.

We have also continued to make crucial discoveries and to publish these findings. We are excited to send out this newsletter so we may update you on our progress. We hope you find the progress and results of our research presented in this newsletter as exciting as we do.

Currently, five studies at the CNIR are recruiting participants, including children with ADHD, ASD and TS, as well as typically developing children. We continue to look for new participants, so please feel free to share this newsletter with your family and friends.

Thank you again for your participation. We hope you find the newsletter helpful and informative.

Sincerely,
Stewart Mostofsky, MD
Director of the Center for Neurodevelopmental and Imaging Research

INSIDE THIS ISSUE:

PARTICIPATE IN RESEARCH

We are actively recruiting for ongoing studies. Email us at **CNIR@KennedyKrieger.org** or visit our website at **KennedyKrieger.org/CNIR** for more information.

Thank you for your participation!

Kennedy Krieger Institute

New in Autism Research

Imitation in Children With Autism

Even as newborns, children love to copy the actions and behaviors of others. As children grow, many practical skills, like brushing teeth with a toothbrush, and social skills, like waving "hello," are learned through imitation.

Studies show that children with autism spectrum disorder (ASD) tend to have a harder time with imitation than their neurotypical peers. Some researchers believe this difficulty could affect how children with ASD learn social and physical skills.

Here at the Center for Neurodevelopmental and Imaging Research (CNIR), we are interested in investigating motor imitation in children with ASD through fun dance movements that range in complexity and speed. Using cutting-edge motion-capture technology, our team, in collaboration with our colleagues at the Center for Imaging Science at The Johns Hopkins University, created and tested a Computerized Assessment of Motor Imitation (CAMI). This new method automatically measures a child's ability to imitate the actions of a model on a computer screen.

In two recently published studies, we applied this technology and discovered that children with ASD have a harder time accurately imitating these dance movements, and that we can predict an ASD diagnosis with up to 90% accuracy using our CAMI method. Furthermore, as poorer imitation was associated with greater ASD symptom severity among children with ASD, we can say that CAMI performance is predictive of ASD severity.

With this as a foundation, we were recently awarded a grant from the Simons Foundation to investigate the reliability of this fun, brief video game and to identify ASD-associated difficulties with motor imitation. We will be enrolling children 6–12 years old with ASD, as well as adults with ASD, 18–40 years old. We hope to use this greater understanding to help guide better ways of detecting ASD-related difficulties and providing therapy to individuals with ASD.

Atypical Processing of Dynamic Visual Information in Children With Autism

The difficulties that children with autism spectrum disorder (ASD) have in imitating others' actions can have profound impact on their ability to learn new skills and engage in social interaction. That is why it is important to understand what contributes to imitation difficulties in people with ASD, and then use that knowledge to guide the development of interventions to help people with ASD learn new skills.

One promising explanation is that children with ASD have difficulty perceiving and tracking rapidly changing visual stimuli—a skill that is important for imitating others. To figure out if this is the case, we developed a video game-like task that requires the children to squeeze a bar with their hand while tracking a target on a

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computer screen. The target is either stationary (static) or moving up and down the screen (dynamic). We found that while children with ASD had no difficulty controlling their hand movements to maintain the static target, they had a lot of difficulty controlling the hand movements needed to track the dynamic target moving up and down the screen.

To follow up on this work, we are now examining whether slowing down the speed of visual feedback helps children improve their ability to track the moving target. The findings from this work can help inform new therapeutic approaches, specifically regarding whether slowing the speed of visual information may be an effective way to teach children with ASD new skills, including learning through imitation. We look forward to updating you on these findings soon!

Now It's Your Turn: Social Imitation and Storytelling

Most of us have the tendency to automatically copy or mirror other people's actions: We often yawn when we see someone else yawn, or want to scratch an itch when we see someone else itching. It is possible that this helps us socialize and communicate better with others.

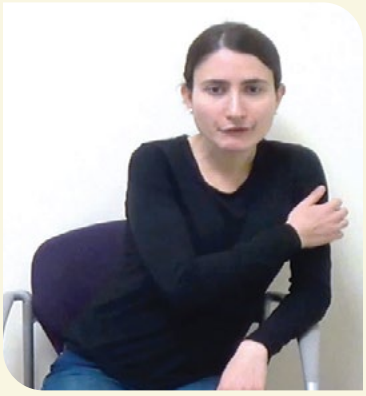
We know that a primary characteristic of autism spectrum disorder (ASD) is a decreased ability to communicate effectively and engage socially with others. This may involve a decreased tendency to copy and imitate others. To explore this further, we investigated how children with and without ASD differ in their tendency to automatically mimic the gestures and movements of a social partner.

For this investigation, we collected data on more than 60 children with and without ASD. Each child watched a video of a narrator who told them an engaging 10-minute story while also doing things such as yawning, scratching an arm and gesturing for emphasis. Each child was then asked to repeat the story to the best of their memory.

We examined whether each child, in retelling the story, was spontaneously imitating the actions and movements they had seen the narrator making. We also analyzed each child's version of the story, looking at, for example, how many details they remembered and how often they used first-person dialogue.

Our next steps include integrating these findings with data from behavioral studies, such as our study of dance imitation, and with neuroimaging data, including data showing differences in the mirror neuron system among study participants. These findings could broaden our understanding of social engagement and communication in children with and without ASD, and could help develop therapies that focus on improving social communication.

Please contact Natalie Alessi at **CNIR@KennedyKrieger.org** for more information on how to participate in one of our ASD studies.



Images to the right, from top to bottom: The actor is yawning. The actor is scratching her arm. The actor is explaining "zooming under the bed" with her hand gesture.

New in ADHD Research

Adolescent Outcomes for Girls and Boys With ADHD

Over the past five years, we have invited adolescents 12–17 years old who participated in research at our center when they were 8–12 years old to return and participate in follow-up studies with us. At the same time, we are also inviting adolescents who have not previously visited our center to participate in research. With this approach, we have begun to make some important discoveries.

In published studies, we have made crucial discoveries about differences in how girls and boys with ADHD progress from childhood to adolescence. We first discovered that from childhood to adolescence, boys with attention-deficit/hyperactivity disorder (ADHD) show greater improvement in cognitive control than girls with ADHD, as compared to same-sex typically developing peers. Furthermore, better cognitive control in childhood predicts a greater reduction in ADHD symptoms from childhood to adolescence. In another published study, we discovered that while both girls and boys with ADHD show subtle motor deficits, boys with ADHD show greater improvement in motor deficits from childhood to adolescence. More recently, we have discovered that girls and boys with ADHD show atypical brain structure across childhood and adolescence, particularly in brain regions involved in emotion regulation. We have also found that girls with ADHD show more persistent increases in emotional symptoms (e.g., irritability, anxiety and depression) from childhood through adolescence, compared to boys with ADHD.

Dr. Keri Shiels Rosch is completing a two-year grant from the National Institute of Mental Health (NIMH) for a project titled "Examination of developmental trajectories of cognitive, motor, and emotional control in relation to sex differences in psychopathology." In this project, Dr. Rosch has combined cross-sectional and longitudinal data from multiple studies conducted at Kennedy Krieger Institute involving children with ADHD from preschool age through adolescence. She is examining how individual differences in motor, cognitive and emotional control—and in associated brain development—relate to sex differences in internalizing disorders, such as anxiety and depression,

and externalizing disorders, such as ADHD, among a sample of children 4–17 years old. For this project, the research team at the Center for Neurodevelopmental and Imaging Research has been developing new methods for characterizing white matter integrity in neural circuity connecting frontal "control" regions and subcortical regions involved in reward and emotional responding, critical for self-regulation. These studies will help us continue to improve our understanding of the development course of ADHD from childhood through adolescence and beyond, including how these trajectories are different for girls and boys with ADHD.

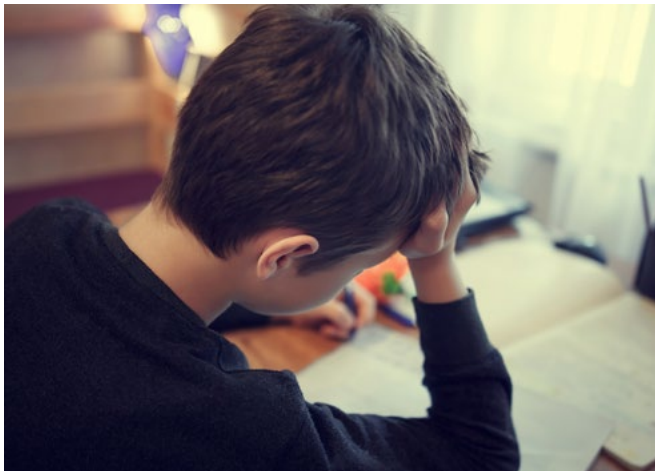
Dr. Rosch recently was awarded a Goldstein Innovation and Collaboration Grant, a two-year internal grant from Kennedy Krieger, for her work on a project titled "Characterizing heterogeneity in decision-making in adolescents with ADHD: considerations of effort, delay, and risk." This project will allow us to look at how, in adolescents with and without ADHD, different forms of decision-making—involving delayed reward, risk-taking and effort—impact behavior and mental health. This important work will allow us to better identify the specific challenges that children with ADHD struggle with, and better target interventions (medication and behavioral) that can address those specific challenges.

Frustration Tolerance in Children With ADHD

One prominent impairment in children with attention-deficit/hyperactivity disorder (ADHD) is emotion dysregulation. Emotion regulation has been defined as an individual's ability to modify an emotional state so as to promote adaptive, goal-oriented behaviors. Prior research suggests that as many as half of children with ADHD demonstrate difficulties with dysregulated emotion. In the long term, emotion dysregulation in children with ADHD is associated with increased severity of core ADHD symptoms (e.g., inattention and hyperactivity/impulsivity), elevated rates of comorbid conditions (e.g., anxiety, depression, oppositional defiant behavior, etc.) and greater social impairment.

At the Center for Neurodevelopmental and Imaging Research (CNIR), we are interested in better understanding the behavioral and neural basis of emotion dysregulation in children with ADHD. In particular, we have focused on two prominent types of emotion dysregulation: frustration and irritability. Our research uses behavioral tasks designed to elicit frustration both in and out of the MRI scanner, as well as questionnaires about children's regulation of emotions such as mood and irritability.

Recent findings from our research suggest the importance of sex differences in frustration and irritability in children with ADHD. Using a novel behavioral task developed at the CNIR, we have found that when frustration is added to a task, girls with ADHD show a significant decrease in their ability to inhibit responses compared to typically developing (TD) girls. In fact, for girls with ADHD, their response inhibition error rate increases by 120% when frustration is added to the task. These results indicate that frustration may not affect all participants equally and may have implications for who is at the greatest risk for negative outcomes due to poor emotion regulation.



Additionally, our research has shown that across adolescence, girls with ADHD show a very different developmental trajectory of irritability than do boys with ADHD or their TD peers. Specifically, while early in development, boys and girls with ADHD show modestly elevated levels of irritability, boys with ADHD show reduced levels of irritability as they progress through adolescence, while girls with ADHD show continued, if not increasing, levels of irritability as they progress through adolescence.

These findings highlight the importance of considering the impact of emotional regulation, particularly irritability and frustration tolerance, for children with ADHD. Next, we plan to continue to examine how emotional dysregulation impacts children with ADHD, both in the short term and in the long term. We also plan to examine how interventions could help children with ADHD better respond to frustrating situations.

Motor and Behavioral Control in Children With ADHD

Children with attention-deficit/hyperactivity disorder (ADHD) are at a substantially increased risk for long-term difficulties into adulthood, in their schooling, jobs and relationships with other people. What is not well understood is how to best identify which children might actually be at risk. One promising approach could be to rely on assessment of motor coordination, which can provide highly reliable tools for pinpointing difficulties with controlling responses.

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It has long been recognized that many children with ADHD show difficulties with controlling motor responses that parallel their difficulties with controlling behavioral responses. Recognizing this, over the past several years, we have worked on identifying highly reliable motor measures that could be used to help better guide ADHD diagnosis and treatment. Our efforts, which were published last year in the journal Neurology, have led to the discovery of two brain-based measures that are abnormal in children with ADHD and, importantly, also predict the severity of ADHD behaviors.

We recently received funding from the National Institutes of Health to build on these findings, taking the crucial next steps to determine whether these two measures, performed with brief and safe transcranial magnetic stimulation (TMS), are reliable and meaningful enough to be used to help improve the precision of individually targeted and effective ADHD treatments. We are actively enrolling children 8–12 years old in this study, including children with ADHD and typically developing children (i.e., without ADHD).

Mindful Movement in Children With ADHD

In a study published last year in the Journal of Developmental & Behavioral Pediatrics, our team at the Center for Neurodevelopmental and Imaging Research (CNIR) found that, for children with attention-deficit/hyperactivity disorder (ADHD), an eight-week tai chi mindful movement intervention was associated with significant improvements in behavior, including in the inattentive and hyperactive/impulsive behaviors that are core to ADHD, as well as in oppositional defiant behavior and disorganization. We also found that the tai chi intervention was associated with significant improvements in motor control and coordination. Finally, we found a significant association of these two findings: The children who showed the most substantial improvements in motor control also showed the most substantial improvements in ADHD behavior.

It is no secret that mindfulness and embodied practices such as yoga and tai chi have enjoyed a steady stream of successes, both in research and in popular media. Many of these embodied practices cultivate sustained attention and the inhibition of distractions and task-irrelevant behaviors—factors that are definitional to the diagnosis of ADHD. Given this, a few years ago, we began a trial of eight weeks of mindful movement training for children with ADHD (two classes per week, for a total of 16 classes). The mindful movement training is focused on tai chi but also incorporates exercises from other embodied practices such as yoga, walking and seated meditations.

Our findings, revealing that mindful movement intervention is associated with improvements in children's attention and behavior, provide support for a promising new avenue of behavioral intervention for children. Therefore, we have extended the scope of our interventions to a wide range of school-age children within Baltimore City public schools, where we are providing mindful movement classes to children during the school day. Our goal is to understand how these interventions can help children improve their abilities to focus and better regulate their emotions and behavior, something that is increasingly challenging for children, particularly since the onset of the COVID-19 pandemic.

In addition, we are continuing to enroll children 8–12 years old with ADHD for our after-school study and are building toward important next steps, including conducting a follow-up study with a control condition to ensure that the positive impact is specific to the mindful movement intervention, as well as conducting studies beyond eight weeks to see if a longer duration of intervention can contribute to both more immediate and sustained improvements in children's ability to better regulate their attention and behavior.

Please contact Alyssa DeRonda at **CNIR@KennedyKrieger.org** for more information on how to participate in one of our ADHD studies.

New in Autism and ADHD Research

Sleep Disturbances in Children With Autism and Children With ADHD

Difficulty with sleep is a common experience for children and can have detrimental effects on school performance, mental health and social functioning. Sleep disturbances are particularly prevalent among children with neurodevelopmental disorders such as attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorder (ASD). Despite accumulating evidence supporting the prevalence of sleep disturbances and their detrimental effects among children with neurodevelopmental disorders, there remains a lot that we do not yet understand.

We have begun to use wearable technology in the form of a simple wristband to get a more accurate, real-time measure of sleep quality and sleep-wake cycles in children. Using both parent ratings and state-of-the-art wearable wristbands to evaluate sleep, our goal is to better understand how sleep is affected in children with neurodevelopmental disorders and how it impacts their ability to function academically, behaviorally and socially.

We are also interested in better understanding the relationship between sleep disturbances and brain development in children with ADHD and children with ASD. In a recent analysis, researchers at the Center for Neurodevelopmental and Imaging Research (CNIR) observed that anomalous connectivity in brain networks relevant to attention and self-reflection was associated with greater parent-reported sleep disturbance in children with ASD. We plan to follow up on these findings using the more accurate wristbands to evaluate sleep quality in children.

We are currently enrolling children 8–12 years old with ADHD and ASD for brain imaging (MRI), with the goal of examining associations between measures of brain structure and function and measures of sleep quality, with measures assessing the core features associated with ADHD and ASD. We hope to gain insight into the nature of sleep quality in children with ADHD and ASD and how sleep is associated with brain development, as well as the impact of these relationships on behavior and academic functioning. Our work could lead to advances in the identification of sleep disturbances and sleep-based interventions, with the potential to reduce the negative impact of sleep disturbances on children's behavioral and social functioning.

Please contact Alyssa DeRonda or Natalie Alessi at **CNIR@KennedyKrieger.org** for more information on how to participate in one of our ADHD or ASD studies.

New in Tourette Syndrome Research

Sensory and Sensitivity in Individuals With Tourette Syndrome

It has long been recognized that people with Tourette syndrome (TS) often report that a sensory "urge," such as an itchy throat, contributes to the need to complete a tic, such as throat clearing. Relatedly, children with TS also may often experience more generalized difficulty ignoring faint, repetitive tactile stimuli. An example of this may be a child being bothered by a tag in their shirt or by seams in their socks.

Recognizing this, we initiated a study to evaluate and compare tactile sensitivity in children with TS to that of typically developing children, to determine whether impaired tactile sensitivity is associated with the severity of tics and sensory urges, and to look into brain mechanisms that contribute to impaired tactile sensitivity and sensory urges in TS.

So far, our findings reveal that, compared to typically developing children, children with TS do show increased tactile sensitivity, with reduced ability to adapt to tactile stimuli. Furthermore, those children with TS who exhibit a reduced range of adaptation also have a greater number of tics.

To examine underlying brain mechanisms, we have employed both brain imaging (MRI) and brain stimulation (transcranial magnetic stimulation, or TMS) methods to examine the function of a key inhibitory brain signal called GABA (short for gamma aminobutyric acid). As we report in recently published findings, we have discovered that among children with TS, reduced GABA-based inhibition in the brain's supplementary motor area (SMA), which is important for selecting and guiding motor responses, is associated with both increased severity of TS symptoms (urges and tics) as well as a reduced ability to actively suppress (i.e., withhold) tics.

We are currently recruiting children with and without TS, 8–17 years old, with the goal of using brain imaging and brain stimulation to confirm whether GABA-based inhibition is reduced in the brain's SMA of children with TS, and to better identify how this is associated with tic severity. The findings will provide a basis for helping children with TS reduce tics and sensory urges by targeting GABA and related brain signaling.

Please contact Jenny Fotang at **CNIR@KennedyKrieger.org** for more information on how to participate in one of our TS studies.

Some of the photographs that appear in these pages are for illustrative purposes only, and any person shown in those photographs is a model.

Interested in participating?

The Center for Neurodevelopmental and Imaging Research is currently enrolling children to participate in several of the studies described in this newsletter. Research participants have the opportunity to complete an IQ assessment and an MRI scan, along with a variety of motor movement games and sensory tasks. Eligible participants will receive monetary compensation for their participation, an IQ report and a picture of their brain! There are minimal risks, such as boredom and fatigue, associated with participation. Please contact a study coordinator at **CNIR@KennedyKrieger.org** if you are interested in learning more about our research studies.

Interested in donating?

This research is funded in part by support from donors and friends of the Center for Neurodevelopmental and Imaging Research. If you would like to learn more, please visit us online at **KennedyKrieger.org/CNIRFund** or contact Jennifer Doyle in the Office of Philanthropy at **DoyleJ@KennedyKrieger.org** or **443-923-4324**.