Center for Neurodevelopmental and Imaging Research at Kennedy Krieger Institute

Dear Families,

Thank you for taking an interest in the Center for Neurodevelopmental and Imaging Research (CNIR) at Kennedy Krieger Institute. I would especially like to thank our research participants and families. Without them, CNIR would be unable to collect data crucial to our mission of better understanding the behaviors and brain circuits that help advance diagnosis and treatment for children with neurodevelopmental disorders, including attention-deficit/hyperactivity disorder (ADHD), autism spectrum disorder (ASD), and reading disability (RD).

For more than twenty years, we have worked with our participating children and families to use behavioral assessments and neuroimaging to better understanding brain-behavioral processes that contribute to cognitive, emotional and motor challenges, and to use that knowledge to pioneer cutting-edge interventions that address these challenges and improve outcomes for children. Additionally, over the past decade we have worked with our participant families to track development into adolescence and even adulthood, providing a crucial opportunity to better understand trajectories contributing to challenges faced by adolescents and young adults.

Most recently, we expanded our research to children with RD and related learning disabilities. In collaboration with our newest faculty member, Dr. Tzipi Horowitz-Kraus, we are examining the effectiveness of an eight-week, web-based reading program. With the support of community partners, like Jemicy School, The Summit School, The New Community School and Baltimore Lab School, we have been able to pilot this program in schools, enrolling children with RD, with ADHD, and with speech and language disorders. Our goal is to identify which language processes contribute to difficulty with reading and to create specialized reading programs for these children.

Currently, we host seven research studies for children ages 2–17 years and two research studies for adults ages 18–40 years. We continue to look for new participants, so please feel free to share this newsletter with your family and friends. Adults and children with ADHD, ASD, or RD are encouraged to join.

We are excited to share our most recent findings with you, below. This progress would not be possible without our participating families. We greatly appreciate all of their support in helping us understand how we can apply science to improve the lives of children with neurodevelopmental differences.

Sincerely,

Stewart Mostofsky, MD

Batza Family Foundation Research Chair

Director, Center for Neurodevelopmental and Imaging Research
Kennedy Krieger Institute

Professor of Neurology and of Psychiatry and Behavioral Sciences
Johns Hopkins University School of Medicine

Research Update – 2023

INSIDE THIS ISSUE:

Kennedy Krieger Institute

CENTER FOR NEURODEVELOPMENTAL AND IMAGING RESEARCH

PROGRESS ON ADHD-FOCUSED STUDIES

Adolescent Outcomes for Girls and Boys with ADHD

Over the past eight years, we have invited adolescents ages 12–17, who participated in research at CNIR 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 continue to make important discoveries building on our previously published work showing that girls and boys with attention-deficit/hyperactivity disorder (ADHD) show different developmental patterns of cognitive control compared to same-sex typically developing peers. Importantly, we have found increasing impairments in cognitive control from childhood to adolescence among girls with ADHD relative to typically developing girls and boys with ADHD. We recently published findings, entitled "ADHD-Related Sex Differences in Emotional Symptoms Across Development" and we have submitted a manuscript being considered for publication showing that girls with ADHD show more persistent increases in emotional symptoms (e.g., irritability, anxiety and depression) from childhood through adolescence, as compared to boys with ADHD.

In addition to these longitudinal findings, we have also collected sufficient data on adolescent clinical and functional outcomes that we have begun to examine childhood brain and behavioral predictors of adolescent clinical and functional outcomes. For example, we have shown that weaker cognitive control and heightened delay discounting (e.g., preference for smaller, immediate rewards over larger, delayed rewards) in childhood predicts greater substance use and anxiety and self-harm, respectively, in adolescents with ADHD. These findings were presented at an international conference and we are preparing a manuscript for publication of these results. We have also submitted findings revealing that measures of brain "wiring" (i.e., "white matter") collected in childhood predict ADHD symptom progression into adolescence. Specifically, children with ADHD with better white matter integrity in corticospinal tracts showed greater improvements in hyperactivity and impulsivity from childhood to adolescence.

Related to this project, Dr. Keri Shiels Rosch recently completed 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 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 CNIR 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. We recently presented these findings at an international conference, showing how developmental changes in white matter integrity of motor circuitry are related to mental health in girls and boys. 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 is progressing towards completing her investigation ,"*Characterizing heterogeneity in decision-making in adolescents with ADHD: Considerations of effort, delay, and risk*," that was supported by a Goldstein Innovation and Collaboration Grant. This project examines how, in adolescents with and without ADHD, different forms of decision-making—involving delayed

reward, risk-taking and effort—impact behavior and mental health. We have collected data from decision-making tasks assessing delay discounting, risk-taking, and effort valuation and are in the process of analyzing these data while we continue to recruit participants. 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.

Please contact **Alec Gonzaga** or **Alyssa DeRonda** at **CNIR@KennedyKrieger.org** for more for more information on how to participate in this study or any other of our ADHD studies.

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 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 and impulsivity), elevated rates of comorbid conditions (e.g., anxiety, depression, oppositional defiant behavior) and greater social impairment.

At 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 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, as compared to typically developing (TD) girls. In fact, for girls with ADHD, their response inhibition error rate increased by 120% when frustration was 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. We also recently submitted a manuscript reporting on the relationship between brain anatomy and emotion dysregulation in children and adolescents with ADHD (ages 8-17), with findings revealing that among girls with ADHD, lower hippocampus (part of the brain associated with memory) volume was associated with higher severity of hyperactive and impulsive symptoms as well as increased difficulty with regulating emotions.

These findings highlight the importance of considering the impact role of emotional regulation, particularly irritability and frustration tolerance, in 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.

Please contact **Alec Gonzaga** or **Alyssa DeRonda** at **CNIR@KennedyKrieger.org** for more for more information on how to participate in this study or any other of our ADHD studies.

Understanding the Co-occurrence of ADHD and Obesity in Childhood

Drs. Rosch and Mostofsky, in collaboration with Dr. Susan Carnell, an associate professor in the Department of Psychiatry and Behavioral Sciences at Johns Hopkins University, are investigating the shared and distinct brain and behavioral basis for ADHD and obesity in childhood. We have collected height and weight data from children and adolescents enrolled in our studies at CNIR to examine associations between behavioral measures of cognitive control and delay discounting (e.g., preference for smaller, immediate rewards over larger, delayed rewards) and body weight, including comparisons of children with ADHD with or without obesity.

We recently published our findings in a paper, entitled "*Neurobehavioral phenotypes of delay discounting and cognitive control in child attention-deficit/hyperactivity disorder and obesity: Shared or distinct?*" The study revealed that typically developing children without a diagnosis of ADHD who are classified as being overweight or obese show a similarly heightened level of preference for smaller, immediate rewards over larger, delayed rewards as children with ADHD, regardless of body weight. In contrast, body weight was not related to cognitive control more generally, suggesting that self-control in the context of reward may be similarly implicated in childhood ADHD and obesity. We are building on these findings to investigate whether emotion dysregulation, including irritability and frustrative non-reward, is similarly affected in children with ADHD and obesity. Our findings, which will be presented at an upcoming international conference, suggest that children with ADHD and obesity show lower frustration tolerance, relative to either condition alone.

Most recently, we have been preparing a conference presentation and manuscript reporting on differences in brain anatomy among school-age children with and without ADHD and who are also obese relative to healthy weight typically developing children. We found that children with ADHD and obesity show the smallest brain volumes in regions of the frontal cortex involved in control functions. In particular, the anterior cingulate, a brain region governing cognitive and emotional interactions, is most affected in children with ADHD and obesity, compared to children with either condition and typically developing healthy weight children. Following up on these findings, we are planning a study that will follow this cohort of children with and without ADHD and who are also obese into adolescence, with the goal of improving our understanding of the brain and behavioral processes that contribute to these prevalent and chronic physical and mental health conditions is important for guiding prevention and intervention efforts.

Please contact **Alec Gonzaga** or **Alyssa DeRonda** at **CNIR@KennedyKrieger.org** for more information on how to participate in this study or any other of our ADHD studies.

Motor and Behavioral Control in Children with ADHD

Children with 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.

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 decade, 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 most recently published in the journal Neurology, have led to the discovery of two brain-based measures that are abnormal in children with ADHD and, importantly, predict the severity of ADHD behaviors.

Based on these promising findings, we received funding from the National Institutes of Health to take crucial steps to determine whether these two brain-based 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 currently enrolling children 8–12 years old in this study, including children with or without ADHD.

Please contact **Alec Gonzaga** or **Alyssa DeRonda** at **CNIR@KennedyKrieger.org** for more information on how to participate in this study or any other of our ADHD studies.

Mindful Movement in Children with and without ADHD

In prior research conducted at CNIR, we found that 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 and oppositional defiant disorder (ODD). We also found that the tai chi intervention was associated with significant improvements in motor control and coordination. Finally, we found a significant association between these two findings: The children who showed the most substantial improvements in motor control also showed the most substantial improvements in ADHD behavior.

Prior research suggests that mindfulness and embodied practices such as yoga and tai chi cultivate sustained attention and the inhibition of distractions and task-irrelevant behaviors—factors that are definitional to the diagnosis of ADHD. Given this information and prior data, our center has collaborated with a local charter school in Baltimore City to further examine the beneficial effects of a mindful movement program. Students in second and third grade at City Neighbors Charter School have been completing a program that introduces them to the mindful movement practices of tai chi. Through the program, children can learn how to identify their emotions and are taught mindful skills that can help them to regulate their emotions and related motor control. The mindful movement training is focused on tai chi but also incorporates exercises from other embodied practices, such as yoga, walking and seated meditations.

The program is facilitated regularly twice a week with students at their school throughout the school year. In addition, students completed assessments at three separate points of time throughout the school year to examine their cognitive and motor control. Parent and teacher questionnaires were also collected to explore changes in observed behavioral control across contexts. Our goal is to understand how these interventions can help students 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.

Our findings from our last cohort that completed the program during the 2021–22 school year reveal participants exhibited improved bilateral motor control as measured by a motor assessment. In addition, students demonstrated improved performance, fewer total errors and a decrease in mean response time as measured by cognitive behavioral tests evaluating executive functions like attentional switching, response speed and response inhibition. Together, these results suggest that the program may be beneficial in enhancing cognitive and motor control.

We are currently building toward expanding the program to include a parent-child, at-home program. The expansion of the mindful movement intervention program to include parent mentors will allow us to assess the impact of parental mentor involvement and the benefit of overall community engagement. We plan in the future to also include a control condition to ensure that the positive impacts observed thus far are specific to the mindful movement program.

For more information on how get your school involved in this study, please contact **Beatrice Ojuri** at: **CNIR@KennedyKrieger.org**

PROGRESS ON AUTISM-FOCUSED STUDIES

Video Game for Assessing Imitation in Children with Autism

Imitation may be the sincerest form of flattery, but it is also a critical learning tool throughout the lifespan. Many practical skills, such as erasing a chalkboard, are picked up through observation. Social behaviors, like waving hello or nodding our heads, are also learned from those around us.

Studies show that ASD children tend to have a harder time with learning through imitation than their typically developing peers. This difficulty could affect how these children acquire social and practical skills.

Here at CNIR, we are interested in investigating motor imitation in children with ASD through fun dance movements. 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 brief (one-minute) video game assessment 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 autism diagnosis with up to 90% accuracy using our CAMI method. Further, we saw that poorer imitation was associated with more severe ASD symptoms among these children, so we can say that CAMI performance is predictive of ASD severity.

These are promising results that reveal the potential of this task to identify ASD-associated difficulties with motor imitation. We are currently enrolling ASD children and adults (as young as 2 years old and as old as 40 years), as well as children and adults without ASD. We are also in the process of looking at what parts of the brain might correlate with imitation performance. In the future, we hope that the CAMI method can be used as a tool to improve diagnosis of ASD and to develop novel imitation-based interventions for helping children with ASD to develop social skills and awareness.

For more information on how to participate in this study or any other of our ASD studies, please contact **Natalie Alessi** at: **CNIR@KennedyKrieger.org**

Atypical Processing of Visual Movement 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 autism, and then use that knowledge to guide the development of interventions to help individuals 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 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 are currently enrolling ASD children and adults (as young as 6 years old and as old as 40 years), as well as children and adults without ASD.

For more information on how to participate in this study or any other of our ASD studies, please contact **Natalie Alessi** at: **CNIR@KennedyKrieger.org**

Intolerance of Uncertainty as a Predictor of Anxiety and Depression in Children with Autism

Anxiety and depression are common and impairing conditions in individuals with autism. Recent evidence indicates that 75% of adults with autism experience an anxiety or depressive disorder, a rate that is significantly higher than the risk of these conditions in individuals without autism. Anxiety and depressive symptoms are associated with withdrawal from enjoyable activities, difficulty completing routines, and reduced performance at school or work. These conditions can also lead to suicidal thoughts and attempts. We do not know what causes high rates of anxiety and depression in autism. If we can identify causes or risk factors, we can develop treatments that could prevent the onset of these conditions.

At CNIR, we have been studying one potential risk factor, intolerance of uncertainty, which is associated with an increased risk of anxiety and depression. Intolerance of uncertainty refers to the tendency to experience strong negative reactions when faced with uncertain situations and events in daily life. Individuals with high levels of intolerance of uncertainty may have difficulty making decisions, adjusting to new situations, or tolerating surprises. Our previous work has shown that intolerance of uncertainty emerges as early as three years old in children with autism. We also found that children who have high levels of intolerance of uncertainty are likely to have anxiety and increased sensitivity to sensory stimuli such as sounds and textures. Additionally, children who have high levels of intolerance of uncertainty do not respond effectively to anxiety treatments. What we do not know is if intolerance of uncertainty at a young age predicts anxiety and depression in later years.

To address this, Drs. Vasa and Keefer, in collaboration with Dr. Mostofsky and with the CNIR team, are launching a preliminary study examining if intolerance of uncertainty during the prepubertal years is linked to anxiety and depression in adolescence and young adulthood. Additionally, our team is interested in learning what brain changes are associated with intolerance of uncertainty in autism. We think that intolerance of uncertainty might be associated with dysfunction within brain networks involving the insula, amygdala, and prefrontal cortex, which play roles in anticipation and threat processing.

In this project, we are reaching out to older adolescents and young adults who participated in a prior CNIR study of intolerance of uncertainty when they were 8-12 years old and inviting them to participate in our follow up study. Participants will complete measures of psychiatric symptoms and a brain scan. The results of this study will lead to a better understanding of intolerance of uncertainty as a risk factor for future psychiatric outcomes and could pave the way for the development of treatments aimed at reducing this risk.

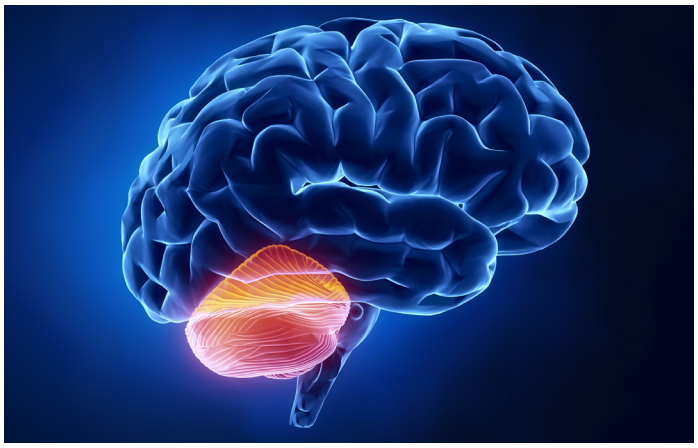
For more information on how to participate in this study or any other of our ASD studies, please contact **Natalie Alessi** at: **CNIR@KennedyKrieger.org**

Understanding How the Cerebellum Contributes to Autism

The cerebellum is one of the most consistently-reported brain areas to show structural and functional differences in autism. Sitting at the back of the head, this region contains over 50% of the cells in the brain and helps to optimize a wide range of behaviors, thoughts and emotions. The cerebellum also helps to guide the organization of neural pathways during early neurodevelopment. How exactly does it contribute to autism?

A compelling hypothesis is that the dentate nucleus, the cerebellum's major channel of communication with the rest of the brain, is structurally and functionally altered in autism. Studies in both humans and autism mouse models suggest that the cerebellar dentate nucleus may not only play an important role in controlling autism-relevant behaviors, it may also be a crucial site for noninvasive brain stimulation (e.g., TMS) to help improve social, communicative and motor behaviors in people with autism spectrum Disorder (ASD).

While there is compelling evidence for the importance of the dentate in autism, visualizing this brain region using traditional MRI methods has been difficult due to its unusual, ribbon-like structure. Fortunately, a new type of MRI scanner at Kennedy Krieger will allow us to address this crucial gap in knowledge: Using innovative methods pioneered by our team at CNIR, we will be



able to examine, for the first time, how dentate nucleus structure and function are affected in children with ASD.

We recently received funding from National Institute of Health (NIH) to use these new MRI methods to study the cerebellar dentate in autism and are now actively recruiting children with ASD, as well as children with ADHD and typically developing children to participate in our study.

For more information on how to participate in this study or any other of our ASD studies, please contact **Laura Rice** at: **CNIR@KennedyKrieger.org**

The Role of Antioxidants and Neurotransmitters in Autism

Researchers have theorized that oxidative stress, an imbalance between the production of reactive oxygen species (free radicals) and antioxidant defenses, may be responsible for some autistic traits[1,2]. Although unwanted, free radicals are a natural result of cells working so our bodies use antioxidants to neutralize them. Furthermore, children are more vulnerable to oxidative stress due to immature cells and higher oxygen consumption[3,4].

The most abundant antioxidant in the brain is Glutathione and it is highly associated with the neurotransmitter, gamma-aminobutyric acid (GABA). GABA is an inhibitory neurotransmitter that helps regulate brain activity.

In this study, we used a novel magnetic resonance spectroscopy (MRS) method to measure both Glutathione and GABA in the brain of children with autism spectrum disorder (ASD) and their typically developing (TD) peers. We chose four specific brain regions associated with autistic traits to measure levels of Glutathione and GABA; these included: 1) Primary Motor Cortex, which is crucial for control and learning actions, 2) Thalamus, which filters sensory and motor information that comes into the brain, 3) Supplementary Motor Area, which is important for motor control and planning and 4) Medial Prefrontal Cortex, which contributes to executive functioning, adaptive behaviors and social cognition.

We found no differences in Glutathione or GABA levels between children with ASD and their TD peers in any of the four brain regions studied. Furthermore, we did not find associations of Glutathione and GABA levels in these regions when looking at measures of autism traits or adaptive (life-skill) functions.

Interestingly, we did find that higher levels of GABA in the primary motor cortex and the thalamus were associated with some ADHD traits, in particular, higher levels of inattention. Another study found similar results, with a connection between attentional difficulties in ADHD and disordered in the GABA system in the brain[5]. These findings contribute to the growing body of knowledge on the neurochemical profiles associated with autism and provide valuable insights into the complex interplay of neurotransmitters and neurochemical signaling.

Although the study found no ASD-group differences in glutathione levels in the brain, previous research has found decreased glutathione levels in the blood of children with ASD[6]. Glutathione is unable to pass the blood-brain barrier, which may explain the lack of differences in the current study. Since this antioxidant is highly important to brain health, brain glutathione levels may be more stable than blood glutathione levels as a protective factor.

This study has come to an end and we are no longer recruiting participants. If you are interested in participating in another Autism study, please contact **Natalie Alessi** at: **CNIR@KennedyKrieger.org**

1. Chauhan A, Audhya T, Chauhan V. Brain Region-Specific Glutathione Redox Imbalance in Autism. Neurochem Res. 2012;37(8):1681-1689. doi:10.1007/s11064-012-0775-4
2. Bjørklund G, Meguid NA, El-Bana MA, et al. Oxidative Stress in Autism Spectrum Disorder. Mol Neurobiol. 2020;57(5):2314-2332. doi:10.1007/s12035-019-01742-2
3. Dringen R. Metabolism and functions of glutathione in brain. Prog Neurobiol. 2000;62(6):649-671. doi:10.1016/s0301-0082(99)00060-x
4. Ikonomidou C, Kaindl AM. Neuronal death and oxidative stress in the developing brain. Antioxid Redox Signal. 2011;14(8):1535-1550. doi:10.1089/ars.2010.3581
5. Mamiya PC, Richards TL, Edden RAE, Lee AKC, Stein MA, Kuhl PK. Reduced Glx and GABA Inductions in the Anterior Cingulate Cortex and Caudate Nucleus Are Related to Impaired Control of Attention in Attention-Deficit/Hyperactivity Disorder. Int J Mol Sci. 2022;23(9):4677. doi:10.3390/ijms23094677
6. Nasrallah O, Alzeer S. Measuring Some Oxidative Stress Biomarkers in Autistic Syrian Children and Their Siblings: A Case-Control Study. Biomark Insights. 2022;17:11772719221123912. doi:10.1177/11772719221123913

Sleep Disturbances in Children with ASD 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 ADHD and ASD. Despite accumulating evidence supporting the prevalence of sleep disturbances and their detrimental effects among children with neurodevelopmental disorders, there remains much 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 questionnaires 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 of the relationship between sleep disturbances and brain development in children with ADHD and children with autism. In a recent analysis, researchers at CNIR observed that anomalous connectivity in brain networks relevant to attention and self-reflection was associated with greater parent-reported sleep disturbance in autistic children. We plan to follow up on these findings using more accurate wristbands to evaluate sleep quality in children.

We are currently enrolling children 8–12 years old with or without 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 **Natalie Alessi** or **Alyssa DeRonda** at **CNIR@KennedyKrieger.org** for more information on how to participate in this study or any other of our ASD or ADHD studies.

PROGRESS ON DYSLEXIA-FOCUSED STUDIES

Reading Fluency in Children with Dyslexia

Dyslexia is a neurodevelopmental learning disorder characterized by reading difficulties (RD), including slow and inaccurate reading that continues into adulthood. The neurological reasons for RD are yet to be discovered, although several differences in how the brain processes written materials have been suggested in previous studies. Individuals with RD may also experience deficits in other cognitive domains. For example, they may struggle with executive functions, an umbrella term used to categorize certain brain processes (e.g., attention, processing speed, working memory, inhibition, etc.) that monitor and optimize our performances when completing tasks. Prior research suggests that individuals with RD can improve their reading skills to some degree if an intervention is provided at an early age. Most reading interventions developed in the past focus on phonological processing and demonstrate an improvement in reading accuracy among individuals with RD. They do not, however, demonstrate much improvement in the reading fluency domain.

At CNIR, we are enrolling children with and without RD in a research study to examine the effects of a computerized reading intervention program that is fluency-based. This program was developed by Dr. Horowitz-Kraus, a faculty member at the Technion–Israel Institute of Technology and Kennedy Krieger Institute, to enhance children's reading fluency skills while building reading speed and developing executive functions. The program improves children's reading by controlling the presentation rate of letters in a sentence that a child reads on a screen. It also examines comprehension skills through questions about the content of the sentence following the removal of the sentence from the screen.

Prior preliminary data has revealed that this program increased reading fluency, reading accuracy and comprehension in children with RD across several age groups. Our study seeks to further examine the effects of this program on reading performance, including reading fluency. We are currently investigating how demonstrated changes in reading performance following completion of this training correlates to changes in the neural circuitry that supports reading and executive functions.

Our study also introduces an executive function "warm-up" prior to starting the reading training. For the warm-up, children complete a program that trains underlying factors of reading processes, such as working memory,

inhibition, visual attention and processing speed. With the introduction of this warm-up combined with the reading program, we can assess alterations in neural circuitry supporting reading in the brain and compare it to alterations in circuitry demonstrated by the reading-only intervention group.

In addition, CNIR has branched out into the community to collaborate with schools in the area that serve student populations with learning disabilities to provide a school-based intervention approach. Through our collaborations, schools have provided their students with the computerized reading program and incorporated it into their school curriculum so students can complete the intervention during their routine school schedule. Our school collaborations have also highlighted the high comorbidity rate of ADHD and dyslexia, which is estimated to be somewhere between 25–40%. Understanding the overlap between these two prevalent developmental disorders is key to elucidating their underpinning neural circuitry, which likely involves shared executive dysfunction. Thus, we have expanded our study to include children with RD who also have an ADHD diagnosis. We plan to examine whether the computerized reading intervention may be most beneficial for children with both ADHD and RD in enhancing their reading performance and executive functioning skills.

For more information on how to participate in this study or any other of our RD studies, please contact **Ramona Sanghvi** at: **CNIR@KennedyKrieger.org**

OPPORTUNITIES FOR PARTICIPATION IN CNIR STUDIES

Interested in Participating?

CNIR is currently enrolling children and adults (ages 2–40) to participate in several of the studies. 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 participating in our research studies. For additional information about our studies, please see our active studies below.

AUTISM STUDIES

Video Game for Assessing Imitation in Children with Autism (for ages 2–12)

- To assess the ability of children with and without ASD to imitate social and motor movements and to train a novel diagnostic algorithm

Understanding How the Cerebellum Contributes to Autism (for ages 6–12)

- To gather high-resolution data on the cerebellum in order to determine function subsections responsible for executive function, motor production and social imitation

ATTENTION-DEFICIT HYPERACTIVITY DISORDER STUDIES

Adolescent Outcomes for Girls and Boys With ADHD (for ages 12–17)

- To learn more about the development of executive functioning, emotional symptoms and behavioral outcomes like substance use, risk taking and mood disorders in adolescents with and without ADHD

Motor and Behavioral Control in Children with ADHD (for ages 8–12)

- To learn more about the effect of stimulant medication on the motor integration system in children with and without ADHD

AUTISM & ATTENTION-DEFICIT HYPERACTIVITY DISORDER STUDY

Sleep Disturbances in Children with Autism and Children with ADHD (for ages 8–12)

- To examine the role of sleep/wake problems in the brain and behavioral development in school-aged children with and without ASD

READING DISABILITIES STUDY

Reading Fluency in Children With Dyslexia (for ages 6–12)

- To investigate the effectiveness of a reading intervention on literacy and reading-related brain activity of children with reading difficulty compared to typical readers

RESEARCH ARTICLES

If you are interested in reading more about our ADHD, ASD, TS and learning disabilities findings, please visit us at **https://bit.ly/3M5UybC** to browse through our extensive collection of lab-published articles.

INTERESTED IN SUPPORTING OUR WORK?

All the research listed in this newsletter is funded in part by support from donors and friends of CNIR. If you would like to learn how you can help support our work, please visit us online at **KennedyKrieger.org/CNIRFund** or contact **Jen Doyle** in the Office of Philanthropy at **DoyleJ@KennedyKrieger.org** or **443-923-4324**.

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