Center for Neurodevelopmental and Imaging Research at Kennedy Krieger Institute

Research Update – Spring 2017

Dear parents, caregivers and research participants,

First and foremost, thank you for participating in our research at the Center for Neurodevelopmental and Imaging Research (CNIR). Without dedicated families like yours, we would not be able to conduct our research. We greatly appreciate all your efforts and hope you and your child enjoyed your participation. We decided to create this newsletter as a way to keep our families and participants up-to-date on our work at CNIR. After all, you put in a lot of effort for our studies, and we want to share with you some of our exciting results!

CNIR is dedicated to better understanding the behaviors and brain circuits involved in neurodevelopmental disorders like attention deficit hyperactivity disorder (ADHD), autism and Tourette's syndrome. We are currently running several funded research projects, described in this newsletter, addressing these disorders with the goal of gaining a better understanding of the mechanisms that contribute to these disorders at a neurobiological level.

The goal of our research is to improve identification and diagnosis of neurodevelopmental disorders and to develop novel therapies and effective interventions for children and adolescents with these disorders. For example, based on our research, we have developed a novel therapy for children with ADHD that uses the age-old practice of tai chi.

We hope you find the results of our research presented in this newsletter as exciting as we do.

We are currently recruiting for six studies at CNIR and are always looking for new participants, so please feel free to share this newsletter with your family and friends. Thank you again for your participation and enjoy the newsletter.

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, **KennedyKrieger.org/CNIR**, for more information.

Thank you for your participation!

Kennedy Krieger Institute
UNLOCKING POTENTIAL

Making Bank! Reward and Motivation in ADHD

As the famous baseball player Yogi Berra once said, "A nickel ain't worth a dime anymore." Well, we here at the Center for Neurodevelopmental and Imaging Research hope that kids like quarters!

In one of our ongoing studies, we are interested in learning about how kids with ADHD anticipate and respond to receiving rewards. While playing a money-making game, children are asked to click a button every time a quarter appears on the screen. Before the quarter comes up, the screen will turn green or red. A green screen means that the quarter will probably stay on the screen for a long time, so it will be easier to get. A red screen means that the quarter will probably stay on the screen for a short time, so it will be harder to get. We want to see whether this information will affect the kids' motivation to get the quarter.

We've found that typically-developing kids respond more quickly to the quarters on the red screen, and more slowly to the quarters on the green screen. Interestingly, we've observed that kids with ADHD tend to respond about as quickly to the quarters on the red screen as they do on the green screen. This finding suggests that children with ADHD process rewards differently than typically-developing children do.

We have also been using transcranial magnetic stimulation, or TMS, in combination with this game. During TMS, we place a magnet on top of the participant's head, above a certain spot in the brain called the primary motor cortex. When we trigger the magnet, we activate the primary motor cortex, which sends a signal to a specific muscle in the hand, making that muscle contract. Using TMS with our money-making game will help us better understand how kids inhibit their movements, such as waiting for the quarter to appear on the screen before clicking on it.

We hope this study will give us insight into the different brain mechanisms at work when kids with ADHD process rewards.

Regulation of Emotions in Children with ADHD

Regulating our emotions can be a challenge for all of us. When we get mad or frustrated, we're able to cope with these emotions better on some days than on others. In general, however, children with attention deficit hyperactivity disorder (ADHD) often have a more difficult time regulating their emotions—both positive and negative—than their typically-developing peers.

Few research studies have examined why this is the case. At the Center for Neurodevelopmental and Imaging Research, we've begun to examine what biological (e.g., brain regions) and behavioral (e.g., difficulties with inhibiting responses) factors might contribute to difficulties with emotion regulation in children with ADHD.

Some recent results from our research show that, compared to typically-developing boys, boys with ADHD have smaller amygdalas (the amygdala is the region of the brain associated with emotional responding) and globus pallidi (the globus pallidus is the region of the brain associated with motivation and reward processing). Interestingly, these brain differences were not seen in girls with ADHD compared to typically-developing girls. Additionally, we found that in boys with ADHD, localized regions of expansion in three brain structures (the globus pallidus, putamen and amygdala) were associated with parent reports of emotion dysregulation, suggesting that abnormalities in these regions may be associated with emotion dysregulation in boys with ADHD.

One of our current research projects builds upon this work by looking at frustration tolerance in children with ADHD. Through this research, we are hoping to gain a better understanding of biological and behavioral factors that may contribute to poor frustration tolerance in children with ADHD compared to typically-developing children.

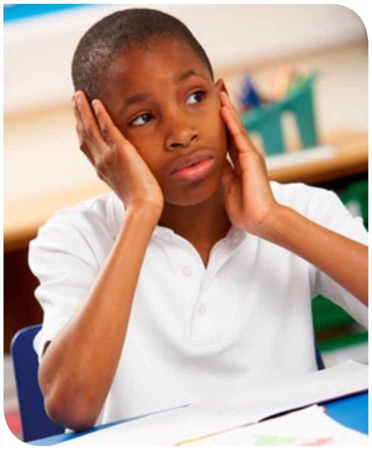
Mindful Movement Training for Kids with ADHD

It's no secret that mindfulness practices have enjoyed a steady stream of successes both in research and the popular media. Many of these practices cultivate sustained attention and the inhibition of distractions and task-irrelevant behaviors—factors that are definitional to the diagnosis of attention deficit hyperactive disorder (ADHD).

This year, we are completing an ongoing trial of tai chi for children with ADHD, and the response from parents and kids alike has been very positive. Going beyond parent and child reports, we are working to identify neural, physiologic and behavioral changes that will help us understand the underlying mechanisms supporting the benefits of mindful movement.

To support our understanding of this tai chi training, we are applying our considerable knowledge of movement-related and "cognitive" (more abstract) mental processes in ADHD as compared to typically developing children. In particular, we are examining changes in the dynamic communication between brain regions using resting-state fMRI, looking at changes in motor cortex inhibition using transcranial magnetic stimulation (also known as TMS), and applying a wide battery of movement and cognitive tests. It's an ambitious project that we're just beginning, but these efforts will help to develop non-pharmaceutical treatments that work in the context of an improved understanding of child development, and the ways that practices like tai chi can scaffold this development.

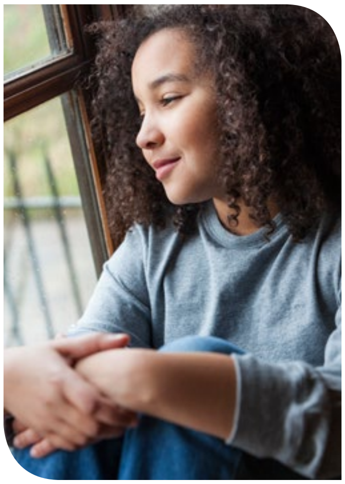
Immediate Gratification in Children with ADHD



While we all tend to prefer immediate over delayed rewards, individuals diagnosed with attention deficit hyperactive disorder (ADHD) are thought to have a particularly strong desire for immediate reward.

In the laboratory, this phenomenon is typically referred to as delay discounting (that is, discounting the value of a reward as it becomes delayed in time) and is often studied by asking individuals to choose between a smaller, immediate amount of money right now or a larger amount of money after waiting for days, weeks, months, or even years. For example, which do you prefer: $5 now or $10 in 1 week? How about $7 now or $10 in 1 week? By changing the amount of the immediate and delayed rewards and the length of the delays, we can get a sense of the degree to which individuals prefer smaller, immediate rewards over waiting for larger, delayed rewards.

We developed a novel task to study delay discounting in children with ADHD involving choices between playing a preferred game independently (e.g., Nintendo DS, Legos, etc.) for a shorter amount of time right away (e.g., play for 30 seconds right now) or a longer amount of time after waiting (e.g., play for 60 seconds after waiting for 100 seconds). Children 8 to 12 years old with ADHD (n=65; 19 girls) and typically developing controls (n=55; 15 girls) performed this task during a visit to our lab. We found that girls with ADHD showed the strongest preference for immediate rewards, whereas boys with ADHD showed a similar preference for immediate rewards as did typically developing boys.



These findings suggest that perhaps girls and boys with ADHD differ in their response to a reward. Furthermore, they emphasize the importance of research on girls with ADHD, who are typically understudied.

Motor Skills and Imitation in Children with Autism

Many children with autism struggle to master a range of motor skills, especially motor skills that require a lot of hand-eye coordination, like catching a ball. The way we learn how to perform a lot of motor skills is similar to the way we learn how to perform a lot of social skills—mainly by visually imitating the actions of other people.

Evidence suggests that children with autism struggle to imitate other people's actions, and many behavioral therapies for autism target imitation skills. However, it is unclear what's going on in the brain to cause these difficulties with imitation. Findings from the Center for Neurodevelopmental and Imaging Research suggest a potential culprit: a bias in the way the brain weighs different types of sensory information. Compared to typically developing children, children with autism trust what they feel through their "intrinsic" sense of touch/body position more than what they see with their "extrinsic" visual sense. This bias may put them at a disadvantage in situations where skill learning is primarily based on visual imitation of the actions of others.

We are currently testing this theory by asking children with autism to imitate novel hand gestures while we record pictures of their brain using a Magnetic Resonance Imaging scanner.

We hope to pinpoint what's different about how the brain of a child with autism 1.) responds to dynamic visual information (e.g., a video of someone else performing a hand gesture) and then 2.) incorporates that visual information into a plan for performing the gesture. Can we help school-age children with autism learn to better imitate the movements of others? And, will being better able to imitate movements also help children with autism better understand and perform gestures during social interactions?

We have developed a video game-like task that asks children to imitate the dance-like gestures of an actor. Children train at slow-motion speeds, which reduces the demand on their brains so that they can process all of the visual information required to learn the dance-like gestures, and then we measure how well they mimic the gestures using an Xbox Kinect motion tracker. We are currently upgrading the way we record children's movements during this task. We're switching from the Kinect system to a motion-capture system that uses markers to record movement, similar to the way in which the tap-dancing scenes in the movie "Happy Feet" and the movements and facial expressions of the passengers on the Polar Express were created.

On the left, a CNIR staff member demonstrates the center's imitation dance task while wearing motion tracker markers. The staff member's corresponding Xbox Kinect image is on the right.

What About the Little Ones?

While we've noticed that school-age children with autism show a bias against "extrinsic" visual information when learning novel movements, we're not sure when this bias develops in the timeline of brain and behavioral changes that lead to a diagnosis of autism.

To explore this question, we're collaborating with labs across the country to study how coordination develops between the visual and motor systems in children who are at high risk for autism because they have at least one older sibling with autism. The way infants learn how to reach and grasp objects offers a unique opportunity to study how visual-motor coordination develops in these at-risk children.

When infants first begin to reach, they swat at toys and have trouble adjusting their hands to accommodate the size, texture or orientation of objects before they make contact with them. Typically, 5-month-old infants rely on touch feedback and align their hands only after making contact with an object, but by 8 months old, infants begin using visual feedback to anticipate how to position their hands while they're still reaching toward an object.

Do infants at a high risk for autism display a delay in making the switch—when reaching for an object—from touch guidance to visual guidance, in comparison to low-risk infants (i.e., those whose older siblings do not have autism)? We've found preliminary evidence from videos of infants playing a ball-rolling game that they do. We observed that at 6 months old, high-risk infants were less likely to move in anticipation of catching a ball before it hit them than low-risk infants were. Now, we're using these videos, along with brain images collected during natural sleep, to explore whether visual-motor coordination during the first year of life is predictive of motor and social abilities during toddlerhood. This project is ongoing, so stay tuned!

What's Next?

We are embarking on an exciting new project to study brain differences between adolescents with and without attention deficit hyperactive disorder (ADHD). We are inviting back participants who previously enrolled in our ADHD studies to see what may have changed since their last visit.

Participants will return to complete many of the same response-control games that they played at their original visits. Each one will also have another MRI and receive an updated picture of his or her brain. If your child is still between 12 and 18 years old, you may soon receive a phone call from us to see if you are interested in participating.

We are also actively recruiting for our brand-new study for children with and without Tourette's syndrome. This study will investigate whether tactile sensitivity plays a role in tic severity. We will also use transcranial magnetic stimulation (also known as TMS) to examine how inhibition in the motor cortex may relate to tic severity. If you know anyone 8 to 12 years old with or without Tourette's syndrome, we'd love to hear from you.

For more information, email us at **CNIR@KennedyKrieger.org** or visit **KennedyKrieger.org/CNIR**.

This research is funded in part by support from donors and friends of CNIR. If you'd like to learn more, please contact Jen Doyle in the Office of Philanthropy at **DoyleJ@KennedyKrieger.org** or **443-923-4324**.