Update

Research Newsletter Summer 2018

Let's Get Physical!

One of the most common co-occurring symptoms for children with autism is anxiety. Chronic anxiety not only can lower quality of life for children and their families, but it can lead to depression as well. While anxiety can be treated with medication with some positive effect, researchers at the Thompson Center are exploring other ways to help reduce anxiety while remaining healthy.

One promising potential way to reduce anxiety is regular physical activity. A recently completed pilot study from the University of California-Irvine showed a reduction in anxiety symptoms in children with autism when they participated in physical activity on a regular basis.

Now, Dr. Lea Ann Lowery, an occupational therapist at the Thompson Center and an associate clinical professor of occupational therapy in the University of Missouri School of Health Professions, is expanding on that study in order to learn more about how well physical activity reduces anxiety in children with autism.

"We know that anxiety can really cause a lot of stress for children with autism as well as their families," Lowery said. "Physical activity not only is important for all children in order to be healthy, but we also think it could have some really positive effects on anxiety as well. This study should help paint a clearer picture about exactly how much effect it can have."

For her study, Physical Exercise to Reduce Anxiety in Autism (PETRA), Lowery hopes to recruit 75 children with autism and anxiety between the ages of 6 and 12. Before participating in the study, the children and their families will complete surveys about anxiety and how it effects them. The researchers also will take saliva samples. This will allow them to measure salivary cortisol levels in each child throughout the study. Salivary cortisol is a biological marker of stress and anxiety. During the study, participants will come to the Thompson Center three times a week for eight weeks to take part in either physical activities, including cardio, strength, jumping, running and obstacle courses, or to play sedentary games such as Minecraft or Legos.

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What's Inside?

Throughout and following the eight-week period, the researchers will continue to measure participants' Body Mass Index (BMI), heart rate levels, flexibility and strength, as well as their levels of anxiety through saliva and surveys to compare the physically active group with the sedentary group

"We really hope to see a reduction in overall anxiety among all our children, as well as some potential physical improvements with their overall health," Lowery said. "Wouldn't it be great if doing something healthy and fun could help reduce anxiety as well? We think that will be the case, but we want to be able to prove it scientifically."

The first cohort of participants for the PETRA study began this summer. The study will take three years and is funded by a grant from the Autism Intervention Research Network on Physical Health (AIR-P). Lowery and the Thompson Center researchers are partnering with researchers at UC-Irvine to conduct the study. Across both sites, researchers hope to recruit 200 children to participate.

Link Found between Neurotransmitter Imbalance, Brain Connectivity in People with Autism

by Eric Maze, MU Health

One in 59 children in the United States lives with a form of autism spectrum disorder, according to the Centers for Disease Control and Prevention. The signs of autism begin in early childhood and can affect individuals differently. However, many with autism share similar symptoms, including difficulties with social communication. Researchers from the University of Missouri School of Medicine and MU Thompson Center for Autism and Neurodevelopmental Disorders identified a link between a neurotransmitter imbalance and brain connectivity between regions of the brain that play a role in social communication and language. The study found two tests that could lead to more precise medical treatments.

"One of the issues with approaching treatment of autism is there are many subtypes and many different genes and potentially other factors that contribute to the disorder," said David Beversdorf, professor of radiology, neurology and psychology at the MU School of Medicine and the Thompson Center. "If you have a treatment that works in one sub-population, it might not work in another.

However, if we can determine why that is, we can pursue individualized approaches and make a lot more progress in developing new treatments."

Using both functional magnetic resonance imaging (fMRI) and proton magnetic resonance spectroscopy (H-MRS), John Hegarty, PhD, while a graduate student in the interdisciplinary neuroscience program at MU and now a postdoctoral fellow at Stanford University, led Beversdorf's team. They investigated the relationship between brain neurotransmitter levels and connectivity of areas of the brain known as the dorsolateral prefrontal cortex and posterolateral cerebellar hemisphere.

Fourteen adolescents and adults with autism spectrum disorder and 12 control participants underwent brain scans. The scans revealed a potential link between functional connectivity, neurotransmitter imbalance, and listening comprehension in individuals with autism. Those with low functional connectivity tended to have a reduced balance of excitatory to inhibitory neurotransmitter levels in the cerebellum and showed impaired listening comprehension, the ability to infer meaning from verbal information. Study participants were administered two questionnaires to determine their autism spectrum disorder-related symptom severity. They also completed two assessments designed to rate different aspects of language and social competence.

"This finding begins to suggest how biomarkers relate with each other in autism," Beversdorf said. "There may be whole other sets of biomarkers that may be inter-related and may be telling us something. It may serve as a biomarker to predict who will respond to what drug."

Study co-authors include John Hegarty, postdoctoral research fellow at the Stanford Autism Center; Dylan Weber, University of Missouri-Kansas City School of Dentistry, and Carmen Cirstea, assistant professor of research at the MU School of Medicine. The study, "Cerebro-Cerebellar Functional Connectivity is Associated with Cerebellar Excitation-Inhibition Balance in Autism Spectrum Disorder," was recently published in the Journal of Autism and Developmental Disorders. Research reported in this publication was supported by a pilot grant from the University of Missouri Brain Imaging Center and the University of Missouri School of Medicine Mission Enhancement Fund.

AIM-ing High

Autism Impact Measure helps show autism treatment impact on children

Many forms of treatment exist that can potentially help improve some social and behavioral deficits for children with autism. However, it is often difficult for autism service providers to determine how successful a treatment is for a specific child.

"Every child is different, so it's important to know what types of treatment do and do not work for each child, based on their specific needs," said Dr. Stephen Kanne, executive director of the Thompson Center. "If a certain behavior therapy or medication is working, it's important for the care provider to know so they can continue the treatment. However, if a therapy isn't working, it's equally important to know, so that the care provider can change what they are doing to better suit the needs of the child."

In order to measure how effective autism treatments are in addressing core autism symptoms, Kanne, along with Dr. Micah Mazurek, formerly on faculty at the Thompson Center and now a professor at the University of Virginia, have developed the Autism Impact Measure (AIM). AIM allows service providers to accurately measure the progress, or lack of progress, their patients and clients are experiencing in terms of improving core autism symptoms.

AIM is a parent-report measure, meaning that parents can fill out questionnaires throughout their child's treatment. AIM has been shown to measure the progress, or lack of progress, in many of the most common types of treatment, including all three major categories of autism treatment: medication-based treatment, behavior therapy-based treatment, and curriculum-based treatment.

"Part of what is valuable about AIM is that it measures both the frequency and the impact of specific autism symptoms." Kanne said. "While we want to know if the child's autism symptoms are improving, it is also important for care providers to know which symptoms are most affecting that child's functioning, so the care provider can be much more effective in providing targeted treatment."

As a culmination of their major National Institutes of Health grant to study the value and effectiveness of AIM, Kanne and Mazurek conducted a final study which found that the AIM measure could accurately indicate whether a patient's core autism symptoms were improving, declining or maintaining the status quo based on the treatment they were receiving.

"Showing that AIM truly measures what we think it does is really important for autism treatment moving forward," Kanne said. "We can now start spreading this measure to autism care providers around the country so they can begin using it to measure the progress of their patients. Ultimately, we hope this will lead to better autism care for everyone."

Genetic targets for ASD identified by MU team

by Jeff Sossamon, MU News Bureau

COLUMBIA, Mo. – A multi-disciplinary team of researchers at the University of Missouri created a new computational method that has connected several target genes to autism. Recent discoveries could lead to screening tools for young children and could help doctors determine correct interventions when diagnosing autism.

"In this study we started with more than 2,591 families who had only one child with autism and neither the parents nor the siblings had been diagnosed with autism," said Chi-Ren Shyu, director of the Informatics Institute and the Paul K. and Dianne Shumaker Endowed Professor in the Department of Electrical Engineering and Computer Science in the MU College of Engineering. "This created a genetically diverse group composed of an estimated 10 million genetic variants. We narrowed it down to the 30,000 most promising variants, then used preset algorithms and the big data capabilities of our high-performance computing equipment at MU to 'mine' those genetic variables."

The genetic samples were obtained from the Simons Foundation Autism Research Initiative. Samples from children with diagnosed cases of autism, and their unaffected parents and siblings were collected leading to more than 11,500 individuals. Using advanced computational techniques, Shyu and his team were able to identify 286 genes that were then collected into 12 subgroups that exhibited commonly seen characteristics of children on the spectrum. Of these genes, 193 potentially new genes not found in previous autism studies were discovered.

"Autism is heterogeneous, meaning that the genetic causes are varied and complex," said Judith Miles, professor emerita of child health-genetics in the MU Thompson Center for Autism and Neurodevelopmental Disorders. "This complexity makes it tough for geneticists to get at the root of what triggers the development of autism in more conventional ways. The methods developed by Dr. Shyu and the results our team identified are giving geneticists a wealth of

targets we'd not considered before—by narrowing down the genetic markers, we may be able to develop clinical programs and methods that can help diagnose and treat the disease. These results are a quantum leap forward in the study of the genetic causes of autism."

This informatics framework is ready for a much larger scale of autism research, such as genetic samples to be collected through the Simons Foundation Powering Autism Research for Knowledge (SPARK), the nation's largest autism study. The study, "Heritable genotype contrast mining reveals novel gene associations specific to autism subgroups," was published in the Journal of Biomedical Informatics. This work was supported by the National Institutes of Health (5T32GM008396, 5T32LM012410-02); the Shumaker Endowment for Biomedical Informatics; the National Science Foundation (CNS-1429294); and the Simons Foundation.

Picking Up the Picky Eaters

A common symptom for many children with autism is food aversion, commonly known as picky eating. This type of extreme picky eating can lead to an unbalanced and unhealthy diet if a child refuses to eat foods such as fruits, vegetables and proteins.

In order to help children with food aversion improve their diet and increase the number of foods they will eat, Thompson Center occupational therapist Brittney Stevenson has developed the Picky Eaters program for patients of the Thompson Center. While the program has existed and had success for several years, Stevenson is now conducting research into exactly how effective the program is at introducing new foods to diets of children with autism.

"Often due to sensory sensitivities or the need for rigid patterns, many children with autism have difficulty adopting new foods to their diet, whether due to their temperature, texture or appearance," Stevenson said. "Some children come into the program eating as few as 7 or 8 different foods, so it's really important to introduce healthy options into their diet."

The Picky Eaters program is designed for preschool-aged children and focuses on structured play activities with food. The program runs from 6-8 weeks and meets once a week at the Thompson Center, though there is an important home component to the program as well.

"The main strategy is to familiarize the children with the look, feel and taste of different foods, primarily vegetables and fruits," Stevenson said. "Once they get comfortable with how a food feels and are convinced it won't hurt them, they start to become more willing to eat that food more regularly."

For her study, Stevenson followed 11 children as they completed the program, tracking how many different foods they would eat before the program and then how many they would eat a few months after the program.

She found that children who participated in the program increased the number of foods they would eat from an average of 17 foods before the program to 25 foods after the program, which is an increase of nearly 50 percent. Stevenson hopes these positive and promising results will continue as she hopes to expand the program.

"Increasing a child's diet, even by 8 different foods, can have a really positive impact on their health and the stress levels of their families," Stevenson said. "It can be easier to go out to eat when you know there will be something on the menu that your child will eat, especially if it is a healthier option."

Stevenson plans to continue studying the effectiveness of the Picky Eaters program in order to ensure she is providing the highest level of service to Thompson Center patients. She also hopes to present the data at the national occupational therapy conference next spring to share her successful methods with other occupational therapists from around the country.

Thompson Center experts find Autism Screener

When a family, doctor or teacher suspects a child has autism, they look to diagnostic experts to determine the diagnosis. However, waiting for a diagnostic appointment can be agonizing – and long. Across the U.S., the average wait time for a diagnostic appointment for autism is 13 months. One solution for speeding up the process of diagnosing children with autism accurately is the use of highly effective screening tools. These tools, if effective, can identify children who are most likely to have an autism diagnosis onto shorter diagnostic waitlists, while those identified as having a lower risk of autism can be funneled into different clinics for more appropriate services, such as for learning disabilities or other disorders.

Now, experts at the Thompson Center for Autism & Neurodevelopmental Disorders have researched the effectiveness of one such autism screening tool, called Cognoa, and found that it is effective in identifying children who are at higher risk for having autism. In a study published in Autism Research, Dr. Stephen Kanne, executive director of the Thompson Center and an internationally recognized expert in autism diagnosis, found that the Cognoa tool maintains an equal level of sensitivity, or ability to detect a risk for autism, as other respected screening tools. However, he also found that Cognoa also has a much higher level of specificity than other screening tools. This means that the tool is better at identifying those children who do not have autism.

"The combination of Cognoa's ability to accurately identify high autism risk while doing a better job of not falsely identifying children who are not at risk makes it a valuable tool," Kanne said. "Being able to more accurately pick out those who truly do have a higher risk for autism makes Cognoa a valuable tool for parents and teachers who don't necessarily have diagnostic expertise."

Cognoa is a smartphone app which allows parents to upload videos of their children responding to predetermined prompts, as well as completing a questionnaire. The app sends the uploaded videos to a group of technicians trained to look for behaviors and symptoms of autism and assign each a numerical code. This data is combined with the parent's responses to the questionnaire, producing the child's score. The higher score the score, the higher the risk the child has for autism. For the study, Kanne tested Cognoa's ability to accurately screen for children with a high-risk of autism through a complex machine-learning algorithm, which produces a score indicating the likelihood that the child has autism.

After first having completed the Cognoa screening process, a group of children ages 18 months to 6 years who were on the Thompson Center's autism diagnostic clinic waitlist participated in the study during a weeklong "blitz" of diagnostic appointments. With clinicians unaware of the Cognoa score from the screening, all 225 children were then given the ADOS-2, which is the gold-standard autism diagnostic test, by diagnostic experts.

The results of the study were promising: Cognoa accurately identified children with a risk for autism 71 percent of the time.

"I believe the app's use of video as well as questionnaires is what allows it to be so specific," Kanne said. "Putting tools such as this one in the hands of parents not only can speed up the time it takes to diagnose children and get them the services they need, but also it empowers families to be a part of the solution themselves."

2018 INSAR in Review

This spring, Thompson Center autism experts joined hundreds of the leading international autism research experts in Rotterdam, Netherlands at the 2018 International Society for Autism Research (INSAR) annual meeting. Every year, INSAR brings together the world's leading autism researchers to present their latest findings and to exchange ideas.

At the conference, several key themes developed. Research is continuing to increase focusing on adults and teens with autism, including their quality of life, mental health, diagnostic tests and differences in sensory processing. Further, research into the genetics involved with autism and co-occurring conditions was often discussed. Specifically, it was announced that the number of genes with strong ties to autism has increased to 99, up from 65 last year. Also, the search for autism biomarkers has increased in recent years.

"The complexity and heterogeneity, or diversity, of autism is being taken into account more broadly," says David Beversdorf, professor of radiology, neurology and psychology at the Thompson Center and the University of Missouri. "This lends emphasis to the need to consider heterogeneity when evaluating the salience of potential biomarkers."

The scope of autism research was another theme of the conference and how researchers should view the scale of their work.

"Some of the biggest takeaways for me were related to how we think about the scope of autism research," said Dr. Karen O'Connor, an assistant research professor at the Thompson Center. "In her keynote, Dr. Geraldine Dawson shared that we need to shift our research paradigm from 'diagnose and treat' to instead 'predict and promote.' I also very much enjoyed the strand focused on females with autism and hearing about the research examining the perspectives of adults with autism related to social camouflaging."

Ultimately, INSAR proved once again to be invaluable as a means of connecting autism researchers and experts, allowing the brightest minds in the field to meet and began innovative collaborations.

"INSAR allowed me connect with some of the leading experts in the field," said Dr. Nancy Cheak-Zamora, an associate professor of health sciences at the Thompson Center and University of Missouri. "I was able to attend a grant writers' luncheon to meet different funding sources. It was a great opportunity to share my grant ideas and I received excellent feedback as well as connections to other funders. Also, conversations during the poster sessions and between meetings was wonderful. I made several researchers with whom I am now working on a collaboration."

In total, the Thompson Center sent 10 staff, students and faculty members to INSAR, and presented 12 posters and research projects at the conference.

Researcher Spotlight: Kerri Nowell

Dr. Kerri Nowell's experiences with disability began early in her life. Growing up as one of six children, Nowell's younger brother was born with a hearing impairment. Nowell credits these early experiences with helping develop her passion for working with children with disabilities.

After growing up in Oman and moving to the United States to attend college, Dr. Nowell spent years working in schools as a school psychologist before pursuing her doctorate in school psychology. Those years of work with autism created an interest, and later a passion, in Dr. Nowell for researching developmental disorders and how they affect children.

Now that she is on faculty at the Thompson Center, Dr. Nowell splits her time between her clinical work, where she assesses and diagnoses children with autism and other neurodevelopmental disorders, and her research.

Dr. Nowell currently is exploring three different research areas: behavioral phenotyping, demographic factors and autism, and young adults with autism and their co-occurring symptoms. Phenotyping involves using multiple sources of information to describe specific characteristics of a child with autism. Dr. Nowell says this could help determine what types of treatments work best for which kids.

"While it is certainly true that every child with autism is different, there is evidence suggesting that we may be able to identify subgroups of children based on shared characteristics," Nowell said. "If we can accurately categorize these symptoms and identify which category a specific child might tend to lean toward, we may be more easily identify the most effective types of treatment for each specific child, rather than having to try many different things before finding what works."

Dr. Nowell also is exploring different demographic factors and how they affect autism and autism diagnosis. She is specifically interested in gender differences in autism and how those differences might affect diagnosis and treatment for girls with autism.

"Because autism seems to affect boys much more often than girls, several of our existing diagnostic tools focus on male behaviors that perhaps girls with autism don't exhibit," Nowell said. "However, there might be more gender-specific behaviors that girls exhibit that are associated with autism that we miss because we are used to looking for behaviors that boys are more likely to show. It is important to identify these female behaviors that may be linked to autism in order to ensure that girls aren't going undiagnosed." Other demographic factors Nowell is exploring include how minority and low-income families access treatment for autism and as well as how what kinds of treatment decisions are made by low-income families and whether those decisions differ from families with higher incomes.

Finally, Dr. Nowell is working to identify and study additional health issues that may affect young adults who also have autism, such as catatonia, anxiety and depression. She currently is the principal investigator on a grant from the Sears Foundation to study the reliability of a catatonia scale developed by Dr. Judith Miles, a long-time Thompson Center researcher.

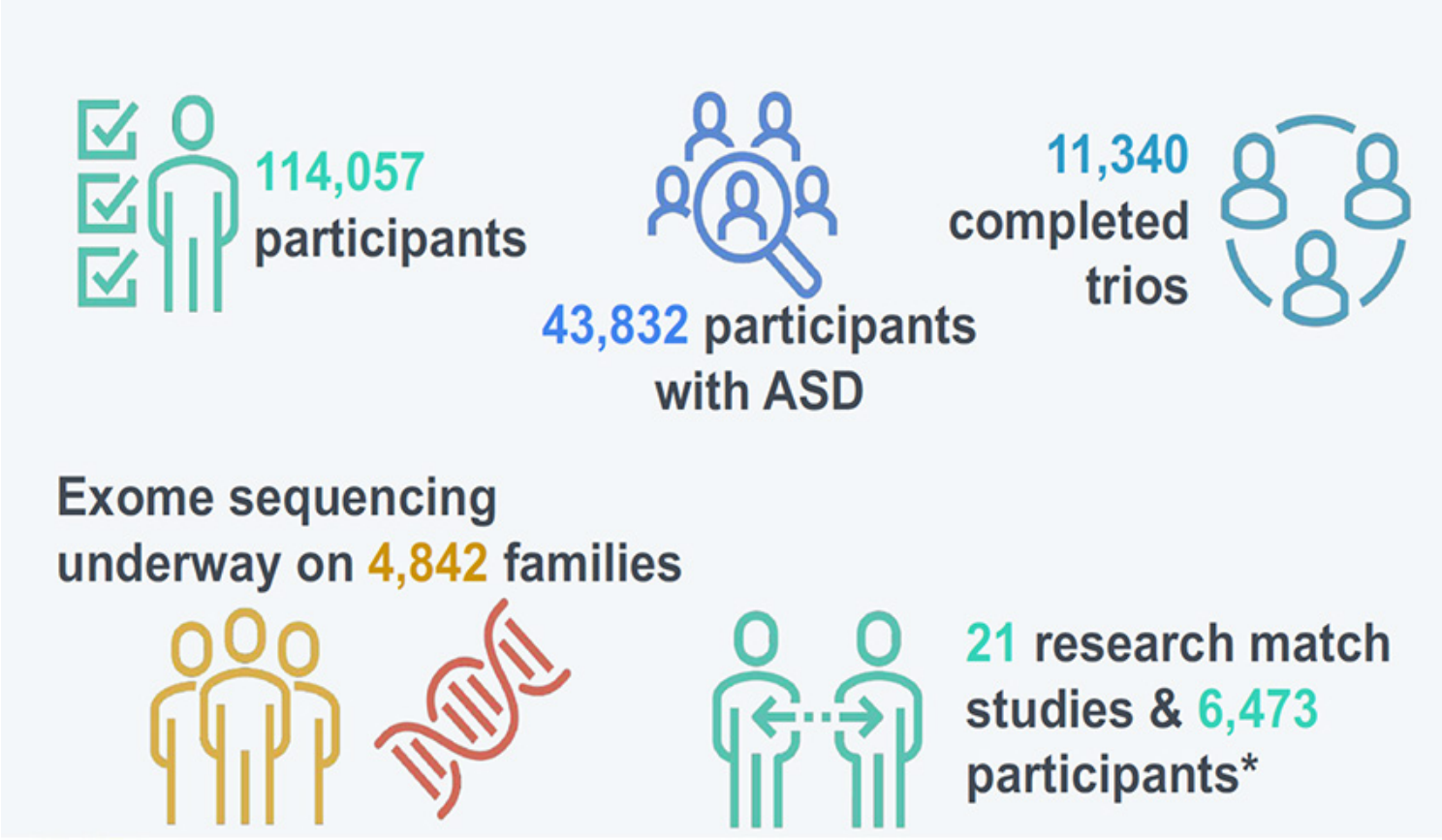
While Dr. Nowell's research interests are broad, her work is targeted toward the same goal: to discover the best ways to identify, care for and support people and families with autism.

A SPARK of Hope

SPARK is a large, online, national research initiative working to bring together a community of individuals with autism and their families. The primary goal of SPARK is to identify the hundreds of genes suspected to be contributing to autism and understand their biological mechanisms.

SPARK also seeks to connect this community of individuals and families to research opportunities that advance the understanding of autism. The Thompson Center is one of 25 sites around the country selected to help recruit participants.

What has SPARK accomplished so far?



What's New with SPARK?

Recruiting participants for autism studies can be extremely expensive and time consuming. In order to hasten our understanding of autism, SPARK has created a new Research Match program, which helps to introduce the 114,000-plus SPARK participants to new research opportunities offered by scientists from around the country.

This process will make it easier for researchers to connect with potential participants, allowing researchers to focus their time and effort on their science, rather than recruitment. The SPARK Research Match program can support many kinds of studies, including in-clinic studies, online surveys, and other types of studies such as remote participation, focus groups and infant sibling studies.

For more information about this program, contact Amanda Shocklee at the Thompson Center, shockleea@missouri.edu or 573-884-6092. To register for SPARK visit www.SPARKforAutism.org/MUTC.

Recent Research Publications

Abbott PW, Gumusoglu SB, Bittle J, Beversdorf DQ, Stevens HE. (2018). Prenatal stress and genetic risk: how prenatal stress interacts with genetics to alter risk for psychiatric illness. Psychoneuroendocrinology 90:9-21.

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Feliciano, P., Daniels, A., Snyder, L., Kanne, S., et al. (2018). SPARK (Simons Foundation Powering Autism Research for Knowledge): a US cohort of 50,000 families to accelerate autism research. Neuron, 97.

Kanne, S., Carpenter, L., & Warren, Z. (In Press). Evaluating a mobile-health screening tool for rapid identification of Autism Spectrum Disorder risk in young children. Autism Research.

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Matsui F, Hecht P, Yoshimoto K, Watanabe Y, Morimoto M, Fritsche K, Will M, Beversdorf D. (2017). DHA Mitigates Autistic Behaviors Accompanied by Dopaminergic Change in a Gene/Prenatal Stress Mouse Model. Neurosci 371:407-419.

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WANT TO HELP?
JOIN A STUDY!

SPARK

SPARK is a free online study with a simple mission: to speed up research and advance the understanding of autism. By building a community of tens of thousands of individuals with autism and their biological family members who provide behavioral and genetic data, SPARK is the largest national autism research study to date.

Participation in SPARK can be done entirely at home. You can register online in 20–30 minutes at: https://sparkforautism.org/?code=mutc.

Enrollment includes completing a few questionnaires and providing a saliva DNA sample using collection kits sent directly to your home. Receive a $50 gift card upon completion of registration process. Find out more about what's involved on our SPARK page: https://thompsoncenter.missouri.edu/autism-research/spark/.

Questions? Contact Amanda Shocklee at:
573-884-6092 or shockleea@missouri.edu

Physical Exercise to Reduce Anxiety in Autism (PETRA)

The primary goal of this study is to evaluate the effectiveness of a physical exercise intervention program to determine its effectiveness in reducing anxiety in children with autism spectrum disorders. This study is specifically targeting underserved children and families.

- Eligibility requirements: Age 6-12 with diagnosis of ASD
- Time required: 1-3 visits over the course of 8 weeks
- Location: Thompson Center
- Monetary compensation: Yes
- Contact: Katie Bellesheim,573-884-8109 or bellesheimk@health.missouri.edu

Trial of Propanolol in Children and Youth with ASD

The purpose of this study is to investigate how propranolol—a drug generally prescribed for high blood pressure—might improve social communication in those with autism. Researchers also will be looking into possible relationships between autism symptoms and how well someone responds to propranolol.

- Eligibility requirements: Age 7-24 with diagnosis of ASD
- Time required: 3 visits over the course of 14 weeks
- Location: Thompson Center
- Monetary compensation: Yes
- Contact: Samantha Hunter, 573-884-6479, huntersg@health.missouri.edu

Interested in being contacted for future studies?
Call 573-884-1893 or email tcresearch@missouri.edu

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