THE UNIVERSITY of NORTH CAROLINA at CHAPEL HILL

2010

AUTISM RESEARCH UPDATE

This newsletter is provided for families and professionals by the UNC Autism Research Program and the Research Registry of the Carolina Institute for Developmental Disabilities. It describes autism research activities at the University of North Carolina.

The Prevalence of Autism is a Hot Topic

What are we learning in North Carolina?

Dr. Julie Daniels, UNC Department of Epidemiology, and colleagues are involved in two CDC funded studies of the epidemiology of autism.

A network of 14 sites across the US monitors the prevalence of autism and evaluates prevalence trends prospectively.

For results and more information see www.cdc.gov/ncbddd/autism/data.html

FAMILIES ARE THE KEY TO AUTISM RESEARCH SUCCESS AT UNC

AN AMAZING CONTRIBUTION

More than a thousand children and adults with autism and their families have participated in at least one UNC autism research study since the Research Registry began in 2001. Many individuals and families have participated in follow up studies or completed more than one study. That is how UNC scientists have been able to make significant contributions the field of autism research. UNC research scientists and their collaborators across North America are making steady progress toward understanding the bio-medical and behavioral aspects of autism spectrum disorders.

KEEPING YOU INFORMED

The goal of this newsletter is to provide a brief progress report on the current research projects at UNC. Space is limited in this publication, but you may request additional information about projects that are of interest.

HOW TO CONTACT STUDIES

Please feel free to call or email me or the project directly. Names, email, and phone numbers are listed in side columns with the names of the projects on the same page as the study's article.

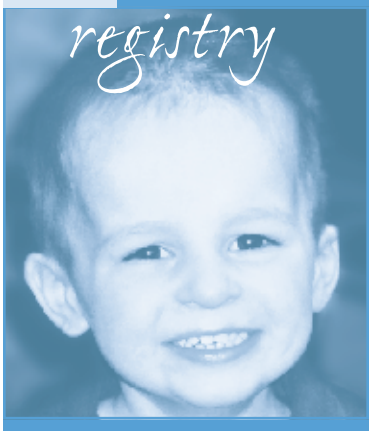
We're Working Together

WE ARE GRATEFUL

On behalf of each one of the research projects, I'd like to express our deep appreciation to the families who contribute to autism research by participating in studies, informing others, and advocating for research funding. It is rewarding for us to work with committed and energetic families who go to extra efforts to improve the quality of life for others affected by autism. It is truly our pleasure.

Renee Clark
UNC Research Registry
Coordinator

The Research registry



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Registry Coordinator

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The UNC Research Registry is a database of individuals and families who are interested in being contacted to participate in studies when they may be eligible. It provides an efficient and confidential way to match potential participants to studies. Currently, there are more than 5,000 individuals (ages 18 months to 70 years old) from across North Carolina in the Registry. At a given time, there are 10-15 studies at UNC actively recruiting participants. The Registry uses age, geographic, and diagnostic information to match and refer Registry members to studies. Typically in a year, a member may get 0-5 study referrals to a variety of types of studies. Study participation is always voluntary and you are never obligated to be in a study.

If you are already a member of the Registry, don't forget to update us if you have a change of address or phone number so we can keep in touch!

Families Are Making a Difference Through Research

IF YOU WOULD LIKE TO JOIN THE REGISTRY, CONTACT US. WE WILL BE GLAD TO SEND YOU AN ENROLLMENT PACKET.

UNC Autism Studies for Families

Extended Families with Multiple Affected Members
Dr. Joe Piven
Visit their website:
http://www.ndrc.unc.edu/familystudy

Social Cognition and fMRI Study
Dr. Joe Piven
Contact: Scott Wallace
scott_wallace@med.unc.edu
1-800-793-5715

Family Studies of Language and Cognition in Autism and Fragile X
Dr. Molly Losh
Visit their website: **http://projects.fpg.unc.edu/cndp/**
Contact:
familystudy@med.unc.edu
1-877-696-5797

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GENETICS AND FAMILY RESEARCH STUDIES

GENETIC STUDY OF EXTENDED FAMILIES WITH MULTIPLE AFFECTED MEMBERS

Dr. Joseph Piven of UNC is collaborating with **Dr. Peter Szatmari** of McMaster University in Canada as they study extended families consisting of multiple branches with a diagnosis of autism. Obtaining more extensive family histories is a new direction for autism research that allows us to research milder manifestations of the genetic liability of autism as well as gather more extensive information concerning genes implicated in autism. DNA samples are examined utilizing the latest technology for genotyping and we hope to identify new regions of the genome which harbor susceptibility genes for autism. Data collection for this study is concluding this winter and we are excited to analyze the data collected. Thank you to all of the families that have participated.

SOCIAL COGNITION AND FMRI STUDY

Drs. Joseph Piven and **Ayse Belger** of UNC are entering their third year of a collaborative NIH funded study with researchers at California Tech and Duke University investigating the neural circuitry in parents of people with autism. Prior research has shown typically developing relatives of people with autism demonstrate language and personality characteristics related to the underlying genetic liability for autism. The hope in this study is to garner a greater understanding into the neural circuitry that may produce these overlapping behavioral characteristics and ultimately new insight into how the brain works in autism. Milder expressions of specific language and personality characteristics in unaffected relatives may reflect focal changes in selected neural circuits that are similar to those in people with autism. The milder expressions are less complicated to identify and will create a basic knowledge to study the more complex neural circuitry in individuals with autism. Preliminary analyses have displayed results correlating to their hypothesis. Recruitment continues for this study for parents of individuals with autism and parents of typically developing children.

FAMILY STUDIES OF LANGUAGE AND COGNITION IN AUTISM AND FRAGILE X

Dr. Molly Losh leads the Carolina Neurodevelopmental Disabilities Project, a group of family studies of autism and fragile X syndrome. Because of strong family support and families' willingness to participate in these projects, Dr. Losh has recently been awarded grants from the National Science Foundation, the National Institute of Mental Health, and the National Institute of Deafness and Communication Disorders to expand this research. This work will include: (1) a study of language in high functioning individuals with autism and their parents, (2) a study of language and social understanding in children with autism and children with fragile X, (3) an investigation of neuropsychological profiles of parents of individuals with autism or fragile X, and (4) genetic analysis examining links between certain behavioral profiles in children and parents, and genetic variation. Together, these studies may help us to better understand the basis of the social and language features of autism and fragile X, their potential overlap, and how the genes involved in these conditions may give rise to subtle characteristics among relatives that are not associated with impairment.

A FAMILY SUPPORT PROJECT: STRENGTHENING MILITARY FAMILIES WITH CHILDREN WHO HAVE DEVELOPMENTAL DISABILITIES

Dr. Irene Nathan Zipper, Director of the Family Support Network at the Carolina Institute for Developmental Disabilities and Dr. Gary Bowen, Professor at the UNC School of Social Work, received a $1 million grant from the federal Administration on Developmental Disabilities for a project to help ensure that military families with children who have developmental disabilities have access to an integrated civilian-military service system that includes state and local resources. Military families must navigate between military and civilian service providers, increasing the challenges they face arranging services for their children. The project is being established at Camp Lejeune with families who live in the area and services will be provided through the Family Support Network of the Crystal Coast. There will be a complete program evaluation to asses the impact of project activities, which include increasing public awareness across the state, and developing a new graduate course to prepare social work students for effective practice with military service members and their families.

EARLY IDENTIFICATION RESEARCH

METHODS AND MEASURES FOR EARLY DETECTION OF AUTISM SPECTRUM DISORDERS

Defining the earliest symptoms of autism and understanding the early course of development of infants at-risk for an eventual diagnosis of autism are essential components toward permitting earlier reliable diagnosis and finding effective treatments for this neurodevelopmental disorder.

Dr. Grace Baranek uses retrospective video analysis methodology to study early development by doing an in-depth study of families' home movies that were taken of children in infancy prior to a clinical diagnosis of autism. Together with other investigators, **Drs. Linda Watson & Betsy Crais,** she has identified early patterns of atypical responsiveness to auditory and visual information, gesture use, and play behaviors that are unique to children who are later diagnosed with autism. Trained evaluators were able to successfully distinguish children with autism from typically-developing and developmentally delayed infants in videos. This project is part of the Sensory Experiences Project, funded by NICHD.

Based on the results of the retrospective video analysis and other empirical findings, Dr. Baranek and her colleagues developed and are refining The First Year Inventory (FYI), a parent questionnaire designed to assess behaviors in 12-month-olds that suggest risk for an eventual diagnosis of autism or related developmental disorders. Other available screeners are designed to begin at 18-24 months. This tool has been translated into other languages and is being used in national as well as international research studies. In addition, the FYI is the basis for a new grant entitled "The Early Development Project" - a three year study conducted by **Drs. Baranek, Turner-Brown, Watson, Crais and Reznick.** This study, funded by Autism Speaks and in its second year, will screen a large sample of infants in the community on their first birthdays in order to identify and further evaluate those who have high-risk scores that may qualify for a new intervention. This randomized controlled trial uses an intervention method called Adapted Responsive Teaching (ART) and compares the experimental group to a community referral and services group. ART interventions are intensive weekly one-to-one sessions that occur in the home environment over the course of 6 months. Children in both the experimental and control groups will receive comprehensive developmental evaluations pre- and post-treatment, and clinical diagnostic evaluations at the age of 30 months, to determine outcomes and test the efficacy of this intervention. The researchers have sent out close to 10,000 First Year Inventories to families in the Triangle on children's first birthdays. From that, they have identified children at risk and assessed numerous families. Many families are currently enrolled in the intervention.

Studies on Early Identification and Risk Factors at UNC

Imaging of Infants at High Risk for Autism
(IBIS Network)
Dr. Joe Piven
Visit their website:
http://www.ibis-network.org/
Contact:
1-800-793-5715
Email:
ibisnetwork@gmail.com

Early Intervention for Children Screened Positive by the First Year Inventory
Dr. Grace Baranek
Visit their website:
http://pearls.med.unc.edu.

Study to Explore Early Development (SEED)
Dr. Julie Daniels
Visit their website:
http://nc-caddre.unc.edu/about_seed

INFANT SIBLINGS BRAIN IMAGING STUDY FOCUSES ON EARLY MARKERS OF AUTISM

The IBIS Network (Infant Brain Imaging Study), which is investigating the brain development of infant siblings at risk for autism, has completed the first year study enrollment. **Drs. Joe Piven** and **Heather Cody Hazlett** direct the team at UNC on this multi-site project. The Network is focusing on the development, behavior, and brain growth in children at high risk for autism (have an older sibling with autism). Recently, the IBIS Network obtained additional funding to examine genetic and environmental factors that could be associated with autism. Approximately 100 six month old "baby sibs" have already participated across the four clinical sites in the U.S., as well as close to 30 controls (typically developing infants, with no family history of autism). Approximately 30 of the 6 and 12 month baby sibs and 18 of the controls were scanned at UNC. The project is in the second year of enrollment and is actively looking for interested families (both those with an older sibling diagnosed with autism and those with no family history of autism). Very little research has been done on infant siblings and an even smaller amount of research has been done on children at 6 months of age who have a family history of autism. This unique study opportunity allows families a glimpse into the clinical perspective of a very essential part of their child's development. Families should expect the following in return for participation: feedback on their younger child's behavior and brain development, payment for participation, and reimbursement for all costs associated with participation in the study.

DEVELOPMENTAL, BEHAVIORAL, AND INTERVENTION RESEARCH

SENSORY EXPERIENCES PROJECT PHASE II

Dr. Grace Baranek, and **Drs. Linda Watson, Brian Boyd, Virginia Dickie,** and **Ayse Belger** launched Phase II of The Sensory Experiences Project (SEP), funded by the National Institute of Child Health & Human Development (Grant# 2R01-HD42168-05), in July of 2008. SEP is comprised of four interacting studies of sensory functioning that will help us explain the development, functional impact, and causes of unusual sensory experiences in children with autism. We are currently enrolling new participants for the following studies:

Study 1, Prospective Developmental Study, is a longitudinal study that examines the stability of sensory features from the preschool (2-6 years) to the school-age (6-12 years) period, and the functional impact of these features on child and family outcomes. The study involves a general battery of child observations, parent questionnaires, and interviews about developmental and sensory features. New participants will receive a free summary of results from developmental and sensory assessments. We are enrolling children with autism, developmental delay, and typical development.

Study 2, Developmental Study of Infants, also know as The Infant Behavior Project (IBP), analyzes videos of the infancy period (9-18 months) of children with autism, developmental delay, and typical development to determine what specific infant behaviors are precursors of established sensory response patterns in the preschool/school-age years and to what extent they predict other developmental and functional outcomes.

Study 3, Observational and Experiential Study, looks at the impact of sensory responses on the daily lives of children with autism, ages 2 to 12 years. We will interview children and their parents and conduct a series of video recorded home observations in natural contexts to learn about children's sensory responses.

Study 4, Neurocognitive Mechanisms, uses electroencephalography (EEG) to measure brain activity during auditory processing in 4 to 12 year old children with autism, developmental delay and typical development. This study will help us understand the causes of unusual sensory reactions to environmental sounds.

Time commitment varies for each participant and study. Financial incentives are based on time requirements and range from $25 to $250.

Thank you to the families who have participated in The Sensory Experiences Project. We truly appreciate your commitment and enthusiasm!

PREDICTING USEFUL SPEECH IN CHILDREN WITH AUTISM

Dr. Linda Watson is collaborating with **Dr. Paul Yoder,** a pre-eminent language researcher at Vanderbilt University, on an NIH funded study focusing on early language development of children with autism. This longitudinal study is recruiting children between the ages of 24 and 47 months and their parents to investigate the factors that affect development of functional speech. Participation includes assessments of language, play, and social skills in the study's conveniently located office in the Research Triangle Park. There are six visits over a period of 16 months. Families will receive $225 for completing the study and reports on their child's progress over time.

STUDY TO EXPLORE EARLY DEVELOPMENT (SEED)

Dr. Julie Daniels and colleagues at 6 sites across the US are conducting a large study to investigate the causes and correlates of autism and developmental delays. The study investigates both genetic and environmental factors that may be involved in the development of autism, specifically focusing on the child's and parents' medical histories and environmental exposures. The study also investigates the extent to which problems with sleep, diet and digestion, and specific physical traits may be more common among children with autism and developmental disabilities. The study is funded by the Centers for Disease Control and Prevention.

Behavioral, Developmental, and Intervention Studies for Children at UNC

The Sensory Experiences Project: Phase II
Dr. Grace Baranek
Visit their website:
http://www.med.unc.edu/sep/project.htm
Contact:
Jeanne Lovmo Murphy
jlmurphy@med.unc.edu

Promoting Early Social-Communicative Competency in Toddlers at Risk for Autism
Dr. Sam Odom
Contact: Martha Lee
leem@mail.fpg.unc.edu
919-962-3982

Predicting Useful Speech in Children with Autism
Dr. Linda Watson
Contact: Ann Firestine
ann_firestine@med.unc.edu
919-558-0200

Language Pragmatics in Children with Autism and FXS
Dr. Molly Losh
Contact: Anne Harris
Anne_harris@unc.edu
1-877-696-5797
Visit their website: **http://projects.fpg.unc.edu/cndp/**

Study to Explore Early Development (SEED)
Dr. Julie Daniels
Visit their website:
http://nc-caddre.unc.edu/

Social Communication and Symbolic Play Intervention for Preschoolers with Autism

Dr. Linda Watson

A curriculum study being conducted in selected classrooms

INVESTIGATIONAL MEDICATION STUDIES AT UNC

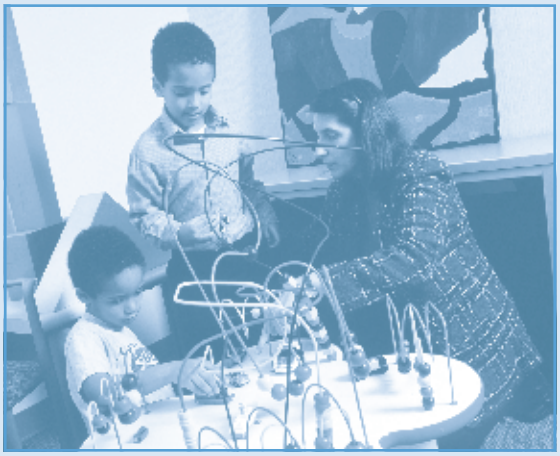
NIH MULTI-SITE MEDICATION STUDY RESULTS RELEASED

On June 1, 2009 the National Institutes of Health announced the results from a study evaluating the effectiveness of citalopram to treat repetitive behaviors in children with autism spectrum disorders (ASD). UNC, under the direction of **Dr. Lin Sikich** was one of the six participating sites. A full report of the 12 week results is published in the Archives of General Psychiatry June 2009 volume 66: 583.

Citalopram, which is sold under the brand name Celexa, is a type of antidepressant called a selective serotonin reuptake inhibitor or SSRI. SSRIs are the type of drug taken most commonly by children and adolescents with autism spectrum disorders (ASDs). Prior to this study, they had only been tested in a limited number of people with ASDs, but have been found to be very effective for treating children with obsessive compulsive disorder, anxiety disorders and depression. The STAART investigators expected citalopram to improve overall functioning in children with ASDs and high levels of repetitive behavior by reducing the repetitive behaviors. The study included 149 children between 5 and 17 years old with ASDs and high levels of repetitive behavior. Seventy-three received citalopram and 76 received a matching liquid that contained no medication called a placebo.

Dr. Sikich explains that what the study found "was that there was no difference in the number of kids who showed a positive response between the citalopram and placebo treated groups." About 1/3 of the kids in each group showed a positive response. However, there were more side effects among the children treated with citalopram. These side effects included increased energy, impulsivity, decreased concentration, increased repetitive movements and behaviors, insomnia, diarrhea and itchy skin. The researchers concluded that citalopram is not an effective treatment for autistic children with repetitive behaviors and that the use of SSRIs in these children "is not without risk." "The obvious short term message is citalopram didn't work, which surprised us a great deal," Dr. Sikich says. "But the really important take home message is that we have to do large, scientifically-sound comparative studies like this to really know whether a specific medication works and is safe. Simply relying on doctors' and families' impressions often leads us to use medications that don't really work for most people with autism and may do more harm to some children," says Dr. Sikich.

Safe and effective medication and behavioral treatments are desperately needed to help children with autism realize their potential and keep from harming themselves or others. Clearly, we need more research to develop and test other interventions for this important problem.



Medication and Imaging Studies at UNC

Autism Treatment and Imaging Study
Dr. Gabriel Dichter
Contact: Ali Rittenberg
amr54@biac.duke.edu
919-951-9513

ASPIRE: Medication Investigational Studies
Dr. Linmarie Sikich
Contact: Cheryl Alderman
aspire@unc.edu
1-800-708-0048

AUTISM TREATMENT AND IMAGING STUDY

Dr. Gabriel Dichter, in collaboration with **Drs. Jim Bodfish** and **Lin Sikich,** is conducting a series of studies examining the effect of medications on brain activity during thinking tasks that require one to pay attention and shift attention frequently. Preliminary work suggests that people with autism and high levels of repetitive behavior show different patterns of brain activity during these tasks than typically developing people. Brain activity is revealed by using functional magnetic resonance imaging before medication is taken and later after 8-12 weeks of treatment.The first drug studied was citalopram. Now Dr. Dichter and colleagues are studying aripiprazole. All individuals participating in the research study will receive free medication (with no placebo) and psychiatric monitoring during the study. They will be reimbursed for travel expenses, and be paid $250 for completing the study. There are also imaging study opportunities that do not involve medication. Dr. Dichter and colleagues believe these studies will help us better understand how specific treatments work in autism.

ASPIRE: ADOLESCENT, SCHOOL-AGE, AND PRESCHOOL PSYCHIATRIC RESEARCH AND EVALUATION PROGRAM

Dr. Lin Sikich and her colleagues at the ASPIRE program are continuing their research to identify and evaluate promising treatments for children and adolescents with ASDs. They have recently completed a study sponsored by Bristol Myers Squibb (BMS) of aripiprazole for children and adolescents with autism and irritable behaviors such as tantrums, aggression and mood swings. Results of this study should be coming out soon. A very similar study also conducted by BMS found that aripiprazole was significantly better than placebo at reducing irritable behaviors in children with autism.

Dr. Sikich is also conducting a year long study of aripiprazole focused on developmental outcomes such as language, cognition and executive functioning. Children and adolescents with ASDs who are not taking medications to improve their autism symptoms and who do not plan to take medications for autism are still needed to provide important comparison information about the developmental progress seen without medication treatment.

The ASPIRE program is also working with other investigators across the country to conduct two different studies of new medications for autism. The first study involves a gastrointestinal enzyme that may be low in some children with autism. The other study is based on similarities between autism and Fragile X syndrome. In fragile X syndrome, a neurochemical pathway in the brain appears overactive and the new medication R-baclofen may reduce activity in this pathway and reduce irritable behaviors like tantrums, self-injury and mood swings.

STUDIES WITH HIGH FUNCTIONING TEENS AND ADULTS

UNC Studies for High Functioning Adolescents and Adults

Tactile Processing Study
Dr. Mark Tommerdahl
Contact: Kristin Burgess
kdburges@med.unc.edu
919-843-2628

Multi-Sensory Imaging Study
Dr. Greg Essick
Contact: Ryan Allred
ryan_allred@dentistry.unc.edu
919-966-5680

Imaging Social and Cognitive Functioning in Autism
Dr. Aysenil Belger
Contact: Dr. Belger
919-843-7368
abelger@med.unc.edu

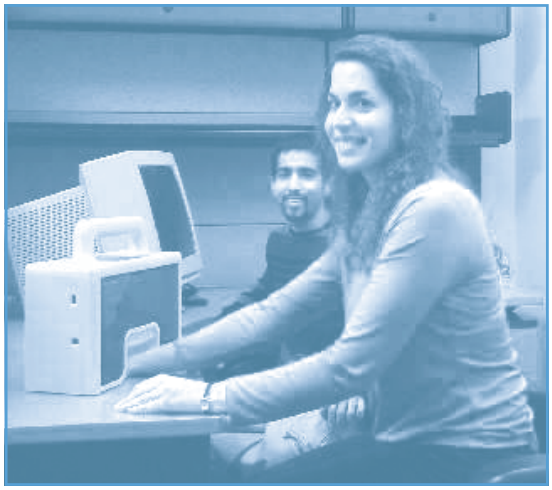
A Study of Sensory and Cognitive Processing in Teens with Autism
Dr. Gunes Yucel
Visit the website:
www.nirl.unc.edu/about_nirl
Contact: Dr. Yucel
gyucel@med.unc.edu
919-843-9665

Psychophysiology of Affective Responses in Autism
Dr. Gabriel Dichter
Contact: Ali Rittenberg
919-951-9513

TACTILE PROCESSING STUDY

Dr. Mark Tommerdahl and **Dr. Grace Baranek** are conducting assessments to measure how individuals with and without autism process sensory information. To accomplish this, tactile (or touch) tasks are employed to study interactions between adjacent and/or near adjacent cortical regions in the brain. Findings from this study suggest that the effects of adaptation on performance during the tactile task are remarkably different for each group. Learning about how people with autism recognize tactile input may lead to improved clinical assessments and contribute to the development of effective treatment for individuals with autism spectrum disorders.

The study is still recruiting adults (ages 18-55) with high-functioning autism or Asperger's.



Demonstrating the vibration sensing task in the Tactile study.

PSYCHOPHYSIOLOGY OF AFFECTIVE RESPONSES IN AUTISM

To better understand emotions in autism, **Dr. Gabriel Dichter** is collaborating with **Dr. James Bodfish** and **Dr. Stephen Benning** of Vanderbilt University to use psychophysiology to investigate how children with autism process emotions. This project is being funded via President Obama's American Recovery and Reinvestment Act (ARRA) of 2009. Responses to pictures of people and objects will be examined via small electromyographic sensors that record imperceptible movements in facial muscles.

Understanding basic emotional processes in autism may shed light on the neurobiological basis of autism symptoms and may elucidate potential benchmarks of treatment response. Pilot data for this study were collected via an internet-based survey conducted in collaboration with the UNC Research Registry. Dr. Dichter and his staff are looking forward to working with families on this exciting project!

MULTI-SENSORY IMAGING STUDY

Dr. Greg Essick and colleagues **Dr. Grace Baranek** and **Dr. Carrisa Cascio** (Vanderbilt University) are conducting the Multisensory Study to understand whether adults with ASD experience sights, sounds, and touch in a way that is fundamentally different from people without ASD. They are also interested in learning how the brain responds to touch in adults with ASD. The study is in its third year and is funded by the Autism Speaks Foundation. Earlier in the study, researchers noted that adults with ASD seem to be more sensitive to heat and vibration against the skin. Currently, participants in the study are experiencing these kinds of touch sensations while researchers measure their brain activity with MRI. Early results of these scans indicate there is a difference in the brain responses in some members of the ASD group; their brain response may turn off faster than adults without ASD for certain kinds of touch. More participants are needed to confirm this finding.

In another part of the study, researchers are looking at how adults with ASD combine sights and sounds into a unified experience. The Multisensory Study is important because it will tell us more about how individuals with ASD perceive simple sensory events. Many people with ASD are highly sensitive to touch, sights, or sounds in their everyday life, but we don't know why, or whether, this is related to other symptoms of autism. Knowing more about this will help us to develop better treatments that address sensory issues in ASD. More participants are needed to confirm these findings, and the Multisensory Study continues to invite adults with autism, aged 18-65, to participate.