The highly successful Early Start Denver Model (ESDM) intervention for children with autism, co-developed by Sally Rogers, professor of psychiatry and behavioral sciences at the UC Davis MIND Institute, has expanded training to more than 20 countries around the world.

The relationship-based intervention for children with autism spectrum disorder (ASD) is provided by trained therapists and parents during natural play and daily routines involving parents and families. It focuses on using play and positive reciprocal interactions to teach a developmental curriculum designed for each child based on their current abilities and interests. It aims to increase the rates of learning across all areas of child development (social-emotional, cognitive and language) for children with ASD as it simultaneously aims to decrease the symptoms of autism.

“While we never foresaw or imagined the kind of international response that our work has stimulated, it demonstrates that all the efforts for earlier recognition of ASD and earlier treatments that our university and so many others have carried out are having a real effect on children and families globally,” Rogers said. “It motivates us to continue to determine how to make our interventions more effective, easier to use and more economical to deliver.”

ESDM trainers have conducted trainings – and continue to train – across the globe in countries including Saudi Arabia, South Africa, France, Germany, Austria, Wales, Italy, Poland, Canada, Sweden, Belgium, Japan, China, Switzerland, Mexico, Brazil, Vietnam, Thailand, India, Spain, Australia and Portugal. The French newspaper *Le Monde* recently featured use of ESDM in Geneva, Switzerland.
Community autism interventions research needed
Quality and types of services vary

With the dramatic rise of children diagnosed with autism spectrum disorder (ASD), the numbers and types of interventions promoted to families and individuals with autism have surged as well.

Aubyn Stahmer, associate professor of psychiatry and behavioral sciences at the UC Davis MIND Institute, emphasized the importance of characterizing and evaluating interventions for individuals with autism recently in the journal *Autism*. An expert in the translation of evidence-based autism treatment to community-based practice and delivery, Stahmer and colleagues Jessica Suhrheinrich and David Mandell make the case that, beyond general facts about services provided, researchers know very little about the types and quality of interventions being delivered to individuals with ASD in the community.

“There are ways to measure the quality of specific interventions, but often providers will combine interventions,” Stahmer said. “And we don’t know if doing that works or how to accurately measure the quality of these combined interventions.”

Stahmer argues that it’s essential for researchers to understand the quality of community interventions for multiple reasons.

The first is to help tailor treatments to different subtypes of autism, which would lead to more effective treatment.

The second is to help identify the necessity of each treatment component and its contribution to an intervention package to help simplify provider training.

Finally, researchers need to measure the quality of care ASD patients receive, as there can be variability in service, she says.

Research Opportunities

The MIND Institute conducts collaborative multidisciplinary research on neurodevelopmental disorders, including autism spectrum disorders, Down syndrome, fragile X syndrome, attention-deficit/hyperactivity disorder and chromosome 22q11.2 deletion syndrome.

For more information about our research and opportunities for participation in studies, contact Brittani Hilscher at 916-703-0299 or bhilscher@ucdavis.edu.

Don’t miss the MIND Institute’s Distinguished Lecturer Series starting in September. For more information, visit ucdmc.ucdavis.edu/mindinstitute/events/dls.
Judy Van de Water said the research also suggests a potential immune profile for the differentiation of autism combined with intellectual disability, as distinct from either autism or developmental disability alone.

“Inflammation during the second trimester in the mothers of children with autism who also have intellectual disability was significantly greater than in mothers of children with autism without intellectual disability in our study,” said Van de Water, who is also director of the UC Davis Center for Children’s Environmental Health. “However, equally significant was that profiles of mothers whose children go on to be diagnosed with autism and intellectual disability differed markedly from those whose children have intellectual disability without autism, as well as from the typically developing general population.

“Their profiles are distinct from all of the other groups that we studied, based on their cytokine and chemokine profiles,” Van de Water continued. “This finding suggests an avenue that we will explore to potentially identify possible markers to separate sub-phenotypes in the autism population.”

The study is published online in Molecular Psychiatry, a Nature publication.

Risk of autism with intellectual disability linked with maternal immune dysfunction during pregnancy

Pregnant women with higher levels of inflammatory cytokines and chemokines, proteins that control communication between cells of the immune system, may be at significantly greater risk of having a child with autism combined with intellectual disability, MIND Institute researchers have found.

Tony Simon, professor in the Department of Psychiatry and Behavioral Sciences, believes it can. Based on 15 years of research, he has invented what looks and functions like a video game but that appears to improve the user’s ability to mentally process information about space and time. These skills are required for activities such as navigating, driving, understanding and learning about numbers and money and telling time.

Children with genetic neurodevelopmental disorders such as chromosome 22q11.2 deletion, fragile X and Turner (Williams) syndromes, have demonstrated dysfunctions in the ability to process information about space and time.

Simon’s approach was based on the knowledge that people who play action video games have sharper resolution in terms of their spatiotemporal cognition. He then worked to develop an algorithm that could measure a person’s spatial and temporal resolution. The research fueled development of the video game, which was built by Funomena LLC, a San Francisco game development firm and supported with a generous donation from the Collison-Russell family. The prototype was designed to adapt its difficulty to each player’s ability based on their spatial and temporal processing capabilities.

Simon has encouraging results from early testing of the prototype. Children with neurodevelopmental disorders improved after playing the game several times. Once a more complete version of the game is complete, researchers will conduct a more complete assessment of the game’s potential to function as therapy.

Digital neurotherapeutic in development

Could a specially developed video game work as therapy for children with certain neurodevelopmental disorders?
Distance language intervention helps adolescents with disabilities communicate

MIND Institute researcher Andrea McDuffie and colleagues have created an intervention involving home-based shared storytelling and real-time parent coaching through telecommunications to help children with fragile X syndrome.

Caused by an inherited genetic mutation that predominantly affects boys, fragile X syndrome is characterized by language delay as well as intellectual disabilities and behavior problems such as trouble paying attention, aggression, anxiety and features of autism. The constellation of problems often makes it hard for a child to express basic needs, engage in conversation or sit still for classroom learning.

In a small but important study McDuffie found that the intervention improved adolescent boys' abilities to produce longer sentences, use more diverse vocabulary and concentrate for longer time periods during conversational interactions.

McDuffie's findings appeared in the American Journal on Intellectual and Developmental Disabilities.

The published study involved three 10- and 11-year-old boys with fragile X syndrome and their mothers. The families were given wordless picture books uploaded onto a tablet, and mothers were coached via Bluetooth headset on strategies to promote more extended and complex conversations while sharing the book with their child.

The study found that for each child, total utterances and the number of new words used increased from baseline to the end of the 12-week study, from nearly doubling to more than tripling. The amount of time each child spent on the sessions also doubled and tripled. The researchers plan to extend the intervention into a larger scale clinical trial that will also provide medications aimed at ameliorating some of the behavioral symptoms of fragile X.
Research links diabetes with anti-fetal brain autoantibodies

Mothers of children with autism who were diagnosed with metabolic conditions during pregnancy, particularly gestational and type 2 diabetes, were more likely to have anti-fetal brain autoantibodies in their blood than were healthy women of children with autism, a study by Paula Krakowiak, a post-doctoral fellow in the UC Davis Department of Public Health Sciences and a researcher affiliated with the MIND Institute, has found.

The presence of these anti-fetal brain autoantibodies has been previously found to be specific to some mothers of children with autism and rare among mothers of children without autism.

In this study, Krakowiak and her colleagues found that diabetic women were three times more likely to have anti-fetal brain autoantibodies, particularly those whose children's autism fell on the severe end of the spectrum. Women with other metabolic conditions, such as high blood pressure and elevated body mass index (BMI), also had a higher prevalence of anti-fetal brain autoantibodies, the researchers found.

“We found a three-fold increase in the prevalence of anti-fetal brain antibodies among the mothers of children with autism who were diagnosed with gestational diabetes or type 2 diabetes,” said Krakowiak.

The research, published online in June in the journal *Autism Research*, was conducted by examining 227 mother/child pairs who participate in the Childhood Autism Risk from Genetics and the Environment (CHARGE) Study.

Earlier MIND Institute research found that approximately 23 percent of women with a child diagnosed with autism had specific patterns of autoantibodies that target proteins highly expressed in the fetal brain. These autoantibody patterns were detected in only 1 percent of women who did not have children with autism. The finding, reported in 2013, was the first to identify a specific risk factor for a significant subset of autism cases, as well as a potential biomarker for drug development and early diagnosis.

SPARK study launches at UC Davis

The MIND Institute was selected to be one of 21 sites for the launch of SPARK, an online research initiative designed to become the largest autism study ever undertaken in the United States.

Sponsored by the Simons Foundation Autism Research Initiative (SFARI), SPARK will collect information and DNA for genetic analysis from 50,000 individuals with autism – and their families – to advance our understanding of the causes of the condition and to hasten the discovery of supports and treatments.

The SPARK effort is being led locally by Leonard Abbeduto, director of the UC Davis MIND Institute, and David Amaral, MIND Institute director of research.

Amaral said the project will undoubtedly change the course of future autism research and hopefully bring practical benefits to affected individuals and families.

“This is the kind of study that the MIND Institute was designed to carry out,” he said.
Autism and cancer share a remarkable number of risk genes

Autism and cancer share more than 40 risk genes, suggesting that common mechanisms underlying the functions of some of these genes could conceivably be leveraged to develop therapies not just for cancer but for autism as well, researchers from the UC Davis MIND Institute and Comprehensive Cancer Center have found.

“This striking coincidence of a remarkably large number of genes implicated in both autism spectrum disorder and cancers has not been previously highlighted in the scientific literature,” said Jacqueline Crawley, MIND Institute distinguished professor and endowed chair. “Potentially common biological mechanisms suggest that it may be possible to repurpose drug treatments for cancer as potential therapeutics for neurodevelopmental disorders.”

“Autism and Cancer Shared Risk Genes, Pathways and Drug Targets,” was published online in Trends in Genetics, a Cell Symposia publication. Crawley collaborated on the work with professor and chair of the UC Davis Department of Microbiology and Molecular Genetics Wolf-Dietrich Heyer, who co-leads the molecular oncology program at the cancer center, and Janine LaSalle, professor of medical microbiology and immunology, who is associated with the MIND Institute.

“Autisms” are best conceptualized like cancers, the authors write: in the plural. Like cancers, the behaviorally defined condition encompasses a broad range of putative causes, symptoms and outcomes. Considerable translational value can be gained from a new focus on understanding the genetic commonalities of autisms and cancers.

“It may be possible to repurpose available cancer drugs with reasonable safety profiles as targeted treatments for ASD,” the authors write. “Stratifying individuals with ASD who harbor a risk gene for autism that is also a risk gene for cancer may enable therapeutic development of personalized medicines based on the specific causal mutation.”

The Center for Excellence in Developmental Disabilities (CEDD) at the UC Davis MIND Institute has received a University Center for Excellence in Developmental Disabilities grant award from the Administration on Intellectual and Developmental Disabilities. The grant, $550,000 per year for five years, extends the work of the CEDD, established in 2006.

CEDD brings added resources to expand the activities and impact of the MIND Institute, serving as a resource in the areas of education, research and service, and providing a link between the university and the community to improve the quality of life for individuals with developmental disabilities.

One of 67 federally designated university centers across the country, the CEDD will use the grant money to address the needs of Californians with developmental disabilities through an expanding range of programs focused on improving health and health care, supporting leadership development and enhancing quality of life, especially in the areas of early intervention and transition to adulthood.
As I reflect back on my first year at the MIND Institute, I feel so fortunate to work with such amazing and dedicated people. Our researchers, clinicians, staff and volunteers are the best and brightest and deeply committed to improving the lives of individuals and families affected by neurodevelopmental disorders.

I’ve met many of our donors over the past few months and heard their stories of why they give. Most are families who have been touched by our work. They are parents, grandparents, siblings, aunts and uncles, friends, neighbors and classmates of children, young adults and adults with neurodevelopmental disorders. Their generosity is motivated by appreciation for the care their loved one received at the MIND Institute and their desire to help find causes, develop improved treatments, provide information and services to families and, ultimately, to develop cures.

Many of our accomplishments are made possible by the generosity of donors, including:
- development of a promising “digital neurotherapeutic,” designed to improve cognitive abilities in children with genetic neurodevelopmental disorders;
- launch of several leading-edge studies, including one of the world’s first clinical trials for fragile X-associated tremor/ataxia syndrome (FXTAS);
- breakthrough discoveries related to ADHD, improved IQ measurements in people with intellectual disability, differences in the brains and behavior of girls and boys with autism;
- recruitment of three early-career investigators focused on autism treatment and genetics related to neurodevelopmental disorders;
- enhancement of our lifespan development in autism program;
- investment in pilot research projects with the potential to lead to significant innovations in treating neurodevelopmental disorders; and
- community programs and lectures including the Lynne Ora Kushel Memorial Lecture on Bipolar Disorder and the “Case of 22q11.2 deletion syndrome: What we have learned about anxiety in children.”

Looking ahead, I am even more excited about what is to come. Len Abbeduto, the director of the MIND Institute, and I will work closely with our MIND Advisory Council and National Council of Visitors, meet with donors and prospective donors to learn more about their interests and discuss ways we can partner to make a difference in the quality of life of people living with neurodevelopmental disorders.

Philanthropy is essential to our institute’s continued success. Thank you to our donors for helping us to make a difference in so many lives.

If you are interested in learning more about donating, please contact me at 916-703-0221 or ekmcbride@ucdavis.edu.
Philanthropy fuels the MIND’s research advances

By Leonard Abbeduto, Director, UC Davis MIND Institute

The MIND Institute continues to make important advances in understanding and treating neurodevelopmental disorders. Our scientists work tirelessly in their labs and in the community, and the institute participates in national partnerships, such as SPARK, to help families. Philanthropy plays a critical role in all of these efforts.

In the most recent pilot grant competition sponsored by the MIND Institute Intellectual and Developmental Disabilities Research Center, two highly innovative projects were selected for funding. Kathleen Angkustsiri, assistant professor of Pediatrics, will study the social impairments associated with 22q11.2 deletion syndrome. Megan Dennis, assistant professor of Biochemistry and Molecular Medicine, will use zebrafish to study genetic mutations hypothesized to create risk for autism in humans. Their goal is to collect preliminary data needed to compete for funding from the National Institutes of Health and private foundations to take these projects even further. Philanthropy has made the pilot grant program possible.

This year the Institute was able to provide funds to help defray the costs of attendance to the annual International Meeting for Autism Research (IMFAR) in Baltimore for 10 graduate students and postdoctoral fellows. IMFAR is the premiere scientific meeting in the field of autism where the latest scientific findings are presented from all over the world ahead of publication. Philanthropy made this support possible.

Philanthropy also makes possible events, programs, and resources for the community, including our public lecture series, Minds Behind the MIND and the Distinguished Lecturer Series. This spring, faculty member Aubyn Stahmer focused her Minds Behind the MIND talk on recently developed evidenced-based educational practices. The April Distinguished Lecturer was Donald Pfaff, of Rockefeller University, who discussed his work on sex differences in autism.

You have helped to advance the mission of the MIND Institute, and we thank you for your generosity on behalf of families affected by neurodevelopmental disorders.