Mutations of a single gene, FMR1 (short for fragile X mental retardation-1) are the triggers for a degenerative disease of the brain that primarily strikes older adults, a form of intellectual disability seen in children and premature menopause. And an FMR1 mutation is the leading single-gene cause of autism.

Now, with the help of a National Institutes of Health (NIH) grant awarded just over one year ago, the M.I.N.D. Institute is unraveling the mysteries of FMR1 by focusing intense attention on one of the disorders that it causes, fragile X-associated tremor/ataxia syndrome, or FXTAS (pronounced “FAX-tass”). Symptoms of this neurodegenerative disease, typically seen in aging males, include tremors and gradual cognitive decline, beginning with memory problems.

Researchers hope that FXTAS will prove to be a Rosetta Stone that will provide deep insight into the origins and potential treatments of all the illnesses associated with mutations of FMR1.

Last year, the same team that discovered FXTAS received nearly $21.8 million from the NIH to develop treatments for it—the largest funding award in history to focus on this or any other FMR1-related disorder.

The five-year grant established the NeuroTherapeutics Research Institute, or NTRI (pronounced “entry”), at UC Davis. The institute serves as the hub of an international research consortium focusing on FXTAS with the expectation that the understanding gained through the study of this illness will be broadly applicable to a host of related disorders.

NTRI is led by molecular geneticist Paul Hagerman, a UC Davis biochemistry and molecular medicine professor who discovered FXTAS with Randi Hagerman in 2001.

“We want to understand all aspects of how FMR1 gene mutations function, not only in FXTAS but also in diseases of the young, such as autism—the full life spectrum of this disorder,” says Hagerman, the lab scientist of the husband-wife research team. “If our aspirations are fulfilled, we’ll eventually be able to develop effective treatments for all the diseases tied to FMR1.”

NTRI Co-director Randi Hagerman

NTRI Co-director Paul Hagerman

If our aspirations are fulfilled, we’ll eventually be able to develop effective treatments for all the diseases tied to FMR1.

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specializes in diagnosing and treating children with fragile X syndrome, the leading heritable form of intellectual disability, adds “Ultimately, we’re really looking for more effective interventions for FXTAS, fragile X syndrome and a wide range of other neurodevelopmental and neurodegenerative diseases.”

To accomplish this goal, the Hagemans have been joined in their research efforts by neuroscientist Robert Berman and cognitive neuroscientists Tony Simon and Cameron Carter. Each is leading distinct teams that share the goal of achieving and measuring therapeutic responses to targeted treatments for FXTAS:

- Paul Hagerman’s team will refine earlier findings on proteins that may be related to the onset of FXTAS to determine which proteins may trigger FXTAS and how.

- Berman’s team is using transgenic mouse models to study the progression of FXTAS and whether or not candidate medications alter the course of the disorder; these mice express the FMR1 mutation that causes FXTAS. Working with Rob Willemsen and other researchers at the Erasmus Medical Center in Rotterdam, The Netherlands, a key consortium partner, Berman is creating a new mouse model allowing the mutant FMR1 gene to be turned on or off under experimental control.

- M.I.N.D. Institute Medical Director Randi Hagerman is leading clinical treatment trials, along with neuroimaging and other electrophysiological tests of the brain changes associated with FXTAS to assess treatment effectiveness.

- Simon’s team is defining the full spectrum of clinical symptoms associated with FMR1, from problems of children with fragile X syndrome to the neurological issues of FMR1 carriers with FXTAS.

- Carter is directing an ambitious Interdisciplinary Training Program in NeuroTherapeutics for postdoctoral scholars in neurotherapeutic research techniques and outcomes, creating a new generation of researchers focused on the translation of molecular discoveries to clinical applications. It brings together trainees from diverse disciplines and backgrounds, including molecular biology, mouse biology and behavior, cognitive neuroscience and human functional neuroimaging; and clinical neuroscience disciplines (neurology, psychiatry, pediatrics and clinical psychology).

Along with the UC Davis School of Medicine, UC Davis Health System and Erasmus Medical Center, other consortium partners are the University of Washington, the University of Colorado Health Sciences Center and Scripps Research Institute. The consortium brings together 19 primary personnel well-versed in collaborative research spanning the disciplines of molecular genetics, cellular neurosciences, animal behavior and neurology, neuropathology, neuroimaging, developmental and behavioral pediatrics, and cognitive neuroscience.

Fragile X syndrome results from a large trinucleotide repeat expansion in a stretch of DNA, or the repeat of the same three nucleotides—cytidine and two guanidines (CGG). Typically, people have about five to 45 of these CGG repeats. The risk factor for FXTAS occurs when the repeat is 55 to 200 times. Fragile X syndrome results when the three nucleotides repeat more than 200 times.

More information about FXTAS, including key symptoms, can be found on the UC Davis NeuroTherapeutics Research Institute Web site at www.ucdmc.ucdavis.edu/ntri and on the National Fragile X Foundation Web site at www.fragilex.org.
Anyone who has worked with children with autism knows that, based on symptoms alone, this disorder is comprised of several different types. Yet, surprisingly, no authoritative study exists to validate this supposition.

That is about to change. For the first time ever, a long-term study of boys and girls with and without autism is being conducted. Jam-packed with scientific evaluations of each participant that will provide data scientists can use for decades to come, this study is destined to determine once and for all if there are subtypes of autism, and, if so, exactly what those subtypes are. And this ambitious study is taking place right here at the M.I.N.D. Institute.

Named the Autism Phenome Project (“phenome” means “all observable characteristics”) it is the largest and most comprehensive assessment of children with autism ever attempted. It aims to distinguish among recognized subgroups, or phenotypes, of autism, linking them with distinct patterns of behavior and biological changes. Ideally, the findings will lead to targeted—and thus more effective—treatments specific to each child’s type of autism.

As co-principal investigator Sally Rogers puts it, “The M.I.N.D. Institute was created to bring scientists together who had expertise among them in all the aspects of autism so that we could look at the whole of autism in a single study, rather than just one part at a time. That’s what the Autism Phenome Project (APP) is all about: parents, children and researchers forming a team to tackle all of autism, at once.”

Led by Amaral, a multi-disciplinary team of more than 50 M.I.N.D. Institute scientists began a pilot study in 2006 of 55 boys and girls aged 2 to 3.5 years, and their families. The project now has more than 150 families, and ultimately is projected to include 1,200 children. The mix will include 800 families with children with autism and 400 families with typically developing children, the latter as a control group.

“If, for example, there are 10 subtypes, then you’re bound to be more certain about your results with 1,000 subjects than with just 100.”

Those 150 children and their families are making an admirable commitment, as will the others who join this longitudinal study in the months to come: subjects are followed for three to eight years via approximately six UC Davis visits the first year and one to two visits in each of the subsequent years.

That first year involves the most exhaustive evaluations, covering everything from medical exams, behavioral assessments and genetic analyses to brain structure imaging, brain function assessments and immune profiling.

“It’s enormously gratifying for me to see how enthusiastic and excited the families are,” explains Amaral, a UC Davis professor of psychiatry and behavioral sciences. “Whether they have children with autism or typically developing children, these families are making an admirable commitment.”

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The logistics of managing a study involving a total of 1,200 families, each with a child who is followed and tested for three to eight years, can be daunting indeed. But the Autism Phenome Project (APP) implementation team is more than up to the task.

Under the guidance of APP Principal Investigator David Amaral, the group is ably led by Project Manager Lou Ann Barnett, with administrative support from Kathy Keihl.

Barnett, whose prior experience includes product development for in-vitro diagnostic microbiology companies, applies a business model to defining processes, management of data and resources involved in the study.

As she puts it, “The APP is a unique example of a cross-disciplinary team in an academic setting. It features not just one or two principal investigators but 16 faculty members, each with differing requirements. Managing competing expectations and multiple lines of communication while building a strong team has certainly been a challenging and rewarding experience.”

Barnett, who holds a Ph.D. in microbiology and immunology from the University of Oklahoma and project management professional certification from the Project Management Institute, oversees seven areas that are handled by one to five staffers each.

Visit Logistics
Research Study Coordinator Kateri Ross, a 2005 UC Davis graduate with a B.A. in psychology, prescreens potential subjects, schedules visits, handles the consent process and initiates medical records for each subject, among many other duties associated with participant selection and visits.

Diagnostic and Behavioral Assessment
Clinical psychologist Lesley Deprey oversees behavioral assessments to determine whether participants meet the study’s eligibility criteria. She’s assisted by four team members in administering a variety of tests with the child and family to assess the child’s development.

Deprey’s team includes psychometrist Lisa Cochran (psychometrists administer and score psychological and neuropsychological tests), psychologist Jane Weru, Parisa Shoja, who handles study questionnaires, and Sarvi Sepehri, who assists with developmental testing.

These staffers are among the first to meet and greet each new family and, as such, are crucial for building rapport with participants.

MRI Group
An important part of APP is the collection of magnetic resonance imaging data on each child during several years of peak brain development (ages 2-4). Getting an MRI can be an unsettling experience for fully functioning adults, let alone for toddlers, many of them with autism, so APP researchers had a special challenge facilitating MRIs for their subjects.

To the rescue came postdoctoral scholar and MRI Lead Christine Wu Nordahl, who crafted a fun experience for kids by building a simulated MRI room filled with games and toys where subjects could hang out for a play date prior to the real thing.

For the MRI itself, her protocol involves a nighttime visit, with the family arriving close to the child’s bedtime. When the child falls asleep after strategically being placed on the MRI bed with a weighted blanket, he or she is sent into the scanner and is imaged while fast asleep.

Nordahl’s team includes: Rob Scholz, whose focus is on tracing images of the amygdala, a part of the brain that’s important in fear processing and memory of emotional reactions; Sarvi Sepehri, who splits her time between the diagnostic and MRI teams; and student assistant Katie Camilleri, who helps conduct the mock MRI visits.

EEG Group
Electroencephalography is the measurement of electrical activity produced by the brain, with the resulting data being used for both research and clinical purposes. In cognitive neuroscience, including autism diagnostics and research, EEG is used to investigate mental activity from low-level perceptual and motor processes to such higher-
order cognition functions as attention span, memory, and reading.

Heading up this important part of APP assessment and data collection is EEG Specialist Margarita Beranksy, aided by fellow EEG Specialist Lindsey Marcelino.

Family Support

Working in tandem with the entire staff, Family Support Liaison Susan Rumberg ensures that participant families have a warm, friendly, and, most importantly, continuous point of contact throughout their several years of involvement in the study.

With a master’s degree in psychology from George Mason University and licensing as a Certified Child Life Specialist, she finds the job to be a perfect blend of her interests and training. “I’m here to serve as a resource,” she says, “to a very committed group of families.”

Her responsibilities range from editing a family support newsletter and preparing families for such procedures as blood draws to responding to individual requests.

“There’s no shortage of ideas,” she quips, “just hours in the day.”

Specimen Handling and Medical Records

Rounding out the implementation team are the Specimen Handling group’s research phlebotomist, Ron Rivera, who oversees the study’s blood draws, and the Medical Records team’s student assistant, Deana Li.

Types of autism (from page 3)

just want to help to find a cure. It’s really a noble goal.”

Rumberg serves as a resource for APP families, her many duties including arranging lodging, securing childcare for subjects’ siblings, and meeting any other needs that participating families might have. Along with her co-workers, she’s the star of a series of videos available online at the study’s Web site (www.ucdmc.ucdavis.edu/mindinstitute/research/app/) designed to walk parents through every step of their involvement with the study.

“I really believe that researchers will be using the data from this study for many years to come,” she adds. “As just one example, every time we do a blood draw, we retain a portion of the blood and DNA in a repository so that this resource can live on for use by researchers in the future, allowing the scientific community to keep making new scientific discoveries.”

Also available to researchers in years to come will be magnetic resonance imaging (MRI) scans of all the subjects’ brains, part of the subjects’ brain function assessments. “Few studies will have so many longitudinal MRIs on kids with autism,” says Amaral. “We’re committed to making these data—and all data acquired by the project—available to the world autism community as rapidly as possible.”

Funding for the project’s approximately $1.2 million per year in expenses has come from a mix of philanthropy, the M.I.N.D. Institute, and, more recently, a portion of a National Institutes of Health (NIH) grant to the Center for Genomic and Phenomic Studies in Autism at the University of Southern California, for which Amaral is co-director.

Amaral and his team are submitting grant applications to the NIH for various aspects of the project; one application, for instance, covers the project’s brain imaging technologies alone. A network of government and philanthropic grants, overlaid with a matrix of collaborations with research institutions around the country, is expected to cover project costs going forward.

“The Autism Phenome Project will produce the integrated data needed to shorten the road to discovery of the causes, prevention and treatments of autism,” says Amaral. “Simply put, the results of this project will make the world a better place for our children and for generations to come after them.”

The project is seeking subjects between the ages of 2 and 3.5 years old, both those with autism and those who are developing typically. For more details, visit www.ucdmc.ucdavis.edu/mindinstitute/research/clinicalstudies.html
2008-09 Distinguished Lecturer Series

Join us for another season of inspiration and ideas from prominent contributors to our understanding of autism and other neurodevelopmental disorders. Lectures are free, open to the public and held in the M.I.N.D. Institute auditorium.

December 10, 2008
Susan E. Levy, M.D.
University of Pennsylvania and The Children’s Hospital of Philadelphia
4 p.m. Are complementary and alternative medical treatments for children with autism evidence-based?
6 p.m. How do or should parents and caregivers choose treatments for children with autism?

January 14, 2009
Pat Levitt, Ph.D.
Vanderbilt University
4 p.m. Translational studies on the MET tyrosine kinase receptor system in the autisms
6 p.m. Where are we with the autisms: an update on genetics and neuroscience advances

February 11, 2009
John L.R. Rubenstein, M.D., Ph.D.
University of California, San Francisco
4 p.m. Patterning in the frontal cortex
6 p.m. Insights into developmental mechanisms that contribute to neuropsychiatric disorders

March 11, 2009
Marshelyn Yeargin-Allsopp, M.D.
National Center on Birth Defects and Developmental Disabilities, CDC
4 p.m. The epidemiology of autism: a global perspective
6 p.m. Autism spectrum disorders: perspectives on surveillance, research and early intervention

April 8, 2009
Andrew W. Zimmerman, M.D.
Kennedy Krieger Institute
4 p.m. Effects of fever in autism: clues to pathogenesis and treatment
6 p.m. The “fever effect” and search for the Holy Grail in autism

May 13, 2009
Thomas Bourgeron, Ph.D.
Institut Pasteur
4 p.m. Synaptic and clock genes in autism spectrum disorders
6 p.m. Toward a better understanding of the genetic susceptibility to autism spectrum disorders

June 10, 2009
Adele Diamond, Ph.D.
University of British Columbia
4 p.m. Prefrontal cortex and developmental neuropsychology: genetic and environmental influences
6 p.m. Cognitive control in young children and ways to improve it

For information about the Distinguished Lecturer Series and to view recordings of past lectures, visit our Web site: www.mindinstitute.org
Bradbury family enrolls two children in the Autism Phenome Project

It takes a five-year commitment—and that’s a long time to commit to anything. But for Erika and William Bradbury, whose two children, Darren, 5, and Lindsey, 4, both are diagnosed with autism, it’s a commitment they’ve been willing to make.

The Bradbury’s five-year commitment is to participation in the M.I.N.D. Institute’s Autism Phenome Project (APP), the largest and most comprehensive study ever mounted of children with autism.

Erika Bradbury understands instinctively the aims of the APP, which is to tease out why each child with autism can seem so very different from another child with the same diagnosis, and why that’s important. She sees it every day in her own two children.

“My daughter Lindsey is very hands off. Nobody touches her. She’s very sensitive to light. She never wanted to be held,” recalled Bradbury, whose family lives in Davis.

“But my son, Darren, is very outgoing. He wanted to be held all the time. He has some tactile stuff but he’s not as severe,” she said.

“Here are two children with the exact same diagnosis and yet they seem so different. How can that be?”

Bradbury said her family became involved in other studies at the M.I.N.D. Institute in 2006. Those experiences led them to enroll in the Autism Phenome Project. With two children on the spectrum, the Bradburys knew that they were in a position to help put the puzzle that is autism together. Their commitment will last another three to five years.

The APP project gathers information about its participants for from five to eight years.

“We knew it was important to help find out about what types of autism there are,” said Bradbury, who is a former college biopsychology major. “We wanted to be able to help with whatever needed to be done.”

Whatever “needed to be done,” has included the Magnetic Resonance Imaging (MRI) studies, blood draws and other medical and developmental evaluations that are a part of the comprehensive APP battery of tests.

But none of that has fazed the Bradburys. Their goal: to gain more knowledge about their own children’s condition—and to help the world gain more knowledge and help all the children like them with autism.

“This gives me a wonderful opportunity to understand,” Bradbury said.

The goals of the Autism Phenome Project are to develop:

- A new system for categorizing distinct kinds of autism
- Novel prevention and treatment strategies for the different kinds of autism
- A database of features that define autism spectrum disorders
- A foundation for future research into the causes of the various forms of autism
- Results that will pave the way for possible cures

To learn more about the project, and how you can become a participant, visit www.ucdmc.ucdavis.edu/mindinstitute/research/clinicalstudies.html
David Hessl: Probing fragile X-associated disorder symptoms and their relationship to autism

The M.I.N.D. Institute is home to many researchers tackling the mysteries of FMR1 (short for fragile X mental retardation-1), the leading cause of inherited intellectual disability. Mutations of the FMR1 gene cause both fragile X syndrome, a neurodevelopmental disorder with striking similarities to autism, and fragile X-associated tremor/ataxia syndrome (FXTAS), a degenerative disease of the brain that primarily strikes older adults. It is hoped that a breakthrough in understanding the mechanisms causing either of these disorders will shed light on the etiologies of the other.

In that spirit Associate Professor of Clinical Psychiatry David Hessl has focused his research on genetic, brain, environmental and neuroendocrine factors affecting cognition and behavior in children and adults with fragile X syndrome and autism. He hopes that, working in tandem with other M.I.N.D. Institute scientists, he can contribute to the understanding of fragile X—a contribution that will have ripples in autism research as well.

Hessl joined the M.I.N.D. Institute in 2002 after earning his doctorate in child clinical psychology at the University of Washington with mentoring from Geraldine Dawson, an internationally known autism researcher now with Autism Speaks, and pursuing postdoctoral studies at UC Berkeley. His training continued at the Behavioral Neurogenetics Research Center at Stanford University, where he began his work on gene-brain-behavior studies in fragile X syndrome with professor Allan Reiss.

“We traveled around the country visiting families of children with fragile X syndrome in their homes to learn about the impact of the environment on their development,” Hessl said. “It was a fantastic opportunity to learn from the children on their own turf when compared to standard meetings in clinical settings. That’s what got me hooked, and it’s the main reason I’m still in the field.”

Hessl said that he couldn’t have chosen a better place to continue his fragile X research.

“Here at the M.I.N.D. Institute, we follow almost 1,000 families with fragile X in their homes to learn about the impact of the environment on their development,” Hessl said. “It was a fantastic opportunity to learn from the children on their own turf when compared to standard meetings in clinical settings. That’s what got me hooked, and it’s the main reason I’m still in the field.”

Hessl has developed a psychophysiology laboratory where he is investigating physiological correlates of emotion and social behavior in children and adults with neurodevelopmental disorders such as fragile X, autism and Down syndrome.

In recent years, his work has focused on premutation carriers of fragile X. “Premutation” refers to a type of gene mutation that doesn’t usually cause mental impairment, although it can lead to psychiatric symptoms. Premutation carriers of fragile X, for instance, are at increased risk for attention deficit hyperactivity disorder (ADHD) and autism as children, and they are at risk for FXTAS as older adults.

His many studies include an examination of amygdala dysfunction in men with the fragile X premutation (the amygdala is a part of the brain that’s important in the processing and memory of emotional reactions). A paper, detailing the results of that study and co-authored by NTRI co-directors Paul and Randi Hagerman, was published last year in the journal Brain.

(continued on page 11)
Presley Knott was something of an enigma to the doctors who initially diagnosed his lack of language, failure to point with his fingers to indicate something that he wanted and limited use of eye contact. Despite these characteristics, which can be symptomatic of an autism spectrum disorder, the 2 ½ year old had met all of his other developmental milestones on schedule.

The diagnosis that made the most sense came from M.I.N.D. Institute Medical Director Randi Hagerman: Presley had a sensory processing disorder. On Hagerman’s suggestion, Presley began undergoing speech and occupational therapy. He had responded well to the therapy, but at around 5 years old, began to exhibit some self-stimulatory behavior and echolalia. Concerned, his parents sought second opinions. Both a neurologist and a psychologist suggested that Presley had autism.

Still, that just didn’t sit well with his parents, according to Presley’s mother, Randi Knott. “Something in our gut told us that, ‘No, that just doesn’t fit,’” Knott said. “I felt like, yeah, we see these new behaviors, but we also had a child who could be in a mainstream preschool and who read non-verbal cues,” Knott said. “It just didn’t add up.”

Since discovering that her son might have a disability, Knott has thrown herself into advocacy for children with neurodevelopmental disorders. She is a Governor’s Appointee to the regional Developmental Disabilities Area Board III and chairs the legislative committee of the State Council on Developmental Disabilities.

It was at one of those meetings that she met Robin Hansen, clinical programs director for the M.I.N.D. Institute, and shared her concerns about Presley. “Robin Hansen walked into the meeting and I burst out crying and said, ‘Can you please help me?’”

After agreeing to see Presley at the Massie Family Clinic at the M.I.N.D. Institute, Hansen, too, was baffled by Presley Knott. “She said she saw an 85 percent ‘neurotypical’ child and 15 percent that didn’t add up,” Knott said. But, undeterred, Hansen evaluated Presley and even visited his preschool and reviewed every family videotape from birth through his fifth birthday party, to try and parse out the enigma that was Presley Knott.

Knott and her husband, Devin, got a call from Dr. Hansen to review what she had learned from her evaluation. “Not only does your child not have autism,” Knott recalled Hansen saying, “He’s not even on the spectrum.” Hansen confirmed Hagerman’s original diagnosis of a sensory processing disorder.

Knott said that the diagnosis was reassuring, and that Presley, who still receives

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M.I.N.D. Institute announces Pilot Research Grants

A major goal of the M.I.N.D. Institute is to foster innovative approaches to understanding autism and other neurodevelopmental disorders, in order to develop new preventions, treatments and cures. To this end, the Institute offers an annual competitive grants program that funds pilot research projects—one-year, small-scale studies designed to test new research ideas, foster collaboration and obtain the preliminary data needed to compete for extramural funding. Increasingly funded through philanthropic donations to the M.I.N.D. Institute, this highly successful program provides awards of up to $25,000 to each recipient.

The M.I.N.D. Institute is pleased to announce the award recipients for its 2008 Pilot Research Grants Program. This year’s funded projects examine a spectrum of relevant research questions, ranging from the effects of autoantibodies found in autism on brain development, to the applicability of event-related potentials, to an evaluation of behavioral control in individuals with attention deficit hyperactivity disorder (ADHD).

We invite you to join us in congratulating this year’s awardees:

- **Robert Berman**, Ph.D., Department of Neurological Surgery, for *Effects of autoantibodies in autism on brain development and behavior in mice*: This study seeks to understand the pathological significance of the autoantibodies found in some children with autism, using a mouse model.

- **Cecilia Giulivi**, Ph.D., Department of Molecular Biosciences, for *Mitochondrial dysfunction in autism*: Several recent studies report a disturbance in energy metabolism in some children with autism, potentially due to a dysfunction of their mitochondria, the cellular site of energy metabolism. This study systematically examines that possibility.

- **Jinoh Kim**, Ph.D., Department of Pediatrics, for *Characterization of function of FMRP in metabolism of amyloid precursor protein*: Animal studies suggest that FMRP, the protein product of the fragile X syndrome gene, regulates production of amyloid precursor protein, a precursor of the toxic peptides that cause Alzheimer’s disease. This study examines whether FMRP plays a similar role in humans.

- **Stephen Noctor**, Ph.D., Department of Psychiatry and Behavioral Sciences, for *Metabotropic glutamate receptor and fragile X mental retardation protein expression in embryonic brain*: Fragile X syndrome is characterized by changes in brain structure. This study examines the role of two proteins in regulating those changes, FMRP which is largely absent, and mGluR5 which is unaffected by this disorder.

- **Clifford D. Saron**, Ph.D., UC Davis Center for Mind and Brain, for *White matter integrity in autism: Electrophysiology of interhemispheric communication and structure-function correlations of the corpus callosum*: Alterations in neural connections between the two sides (hemispheres) of the brain are hypothesized to cause the complex behavioral phenotype of autism. This study uses sophisticated electrophysiological measures to evaluate the functioning of these interhemispheric connections in children with autism.

- **Julie Schweitzer**, Ph.D., Department of Psychiatry and Behavioral Sciences, for *Neural Correlates of Response Preparation, Conflict Detection and Subsequent Performance Adjustment in ADHD via Event-Related Potentials*: Individuals with ADHD are often characterized as making poor decisions because they fail to use environmental cues to guide their behavior or learn from previous mistakes. Little is known about the neural mechanisms associated with these perceptual or cognitive impairments. This study tests the feasibility of using event-related potentials to characterize these two components of decision-making in individuals with ADHD.

- **Marjorie Solomon**, Ph.D., Department of Psychiatry and Behavioral Sciences, for *Is Being a Boy a Risk Factor for Developing Autism?: Neuropeptides and Autism*: One biological explanation for the differential prevalence of autism in males versus females (4:1) is that the female neuroendocrine system, particularly the oxytocin and vasopressin system, confers “protection” against autistic traits. This study seeks to test that hypothesis.

- **Flora Tassone**, Ph.D., Department of Biochemistry and Molecular Medicine, for *Association between folate-dependent genes and autism spectrum disorder*: Maternal folate status and child folate-pathway genes have both been implicated as important factors in neurodevelopmental outcomes. This study will investigate whether and how variations in key genes involved in folate metabolic pathways in a child are associated with autism individually and as they interact with the mother’s folate status during pregnancy.
Diagnostic expertise (from page 9)

speech, occupational and integrated play therapy, is in a full inclusion kindergarten and mainstream soccer and continues to do well. She said that she is deeply grateful for the diagnostic services at the M.I.N.D. Institute, which helped her to understand her son’s condition—and most importantly, how to help him.

“It’s just as important to find out what your child doesn’t have as to figure out what he does have,” Knott said of her son, who’s now 5 ½, noting that “Now, we knew that he was capable of so much more. This will allow us to challenge him to be everything that he can be-everything he wants to be,” she said.

“I think it took a developmental pediatrician to dig deeper and come up with the appropriate diagnosis. The other doctors did what they could accurately, but didn’t have the expertise to evaluate Presley’s situation.”

Grateful for the expertise and insight that Hansen and others brought to her son’s case, as well as the help they have given to the many friends of Presley’s who are on the spectrum, Knott decided to make her 40th birthday party a fundraiser for the M.I.N.D. Institute. Held on Aug. 21, and attended by approximately 120 people, the Las Vegas ‘Rat Pack’-themed event raised nearly $20,000 for M.I.N.D. Institute research.

“It’s tough times out there,” Knott said of the current economic climate, “but I would just hope that people will continue to give. We have one in 150 people who are facing the challenge of an ASD and most of them are boys. We need to help these young men to become everything that they can be and channel their gifts to allow them to live their lives to their fullest potential.”

“I would lend my name to anything that supports the mission of the M.I.N.D. Institute,” Knott said. “I want as many families as possible to benefit in the same way that I have.”

The gift that keeps giving

The holidays are just around the corner! As you think about year-end giving, consider the following ideas:

- In lieu of holiday gift exchanges, consider a financial gift to the M.I.N.D. Institute, in honor of your staff or business colleagues.
- Consider the M.I.N.D. Institute in your estate plans.
- A gift of cash, stock, securities, real estate, or other tangible personal property provides our programs with enduring endowment support.
- Contribute to the M.I.N.D. Institute in honor of a family or loved one.
- The M.I.N.D. Institute recognizes the commitment and dedication of the children and their families who participate in the many clinical research studies conducted at the Institute. To honor their efforts, a ‘thank you’ party is held where we provide a festive, safe and secure setting for children with neurodevelopmental disabilities and their families. Help us fund this very special celebration.

In all cases, the honorees or family will be notified that a gift has been made, but the amount of the gift will remain confidential.

Your gift to the UC Davis M.I.N.D. Institute qualifies as a charitable deduction for federal tax purposes as permitted by law. For more information on how you can make the season especially meaningful, contact Development Officer Terri Contenti at (916) 703-0289, or www.mindinstitute.org

David Hessl (from page 8)

“A surprising but intriguing finding of the study was that these men had reduced amygdala activity when processing social-emotional stimuli, a finding that has previously been reported in adults with autism spectrum disorders,” said Hessl.

Hessl’s laboratory has shown that children with fragile X syndrome have significant deficits in prepulse inhibition (PPI). PPI, which may also have relevance for understanding some symptoms of autism, taps into the brain’s ability to filter out otherwise overwhelming sensory information.

Hessl and his colleagues at several sites in the U.S. and abroad are now using this measure to help document the efficacy of new targeted treatments for fragile X syndrome.

“With the large amount of resources now being devoted to understanding FMR1, especially recent major developments of novel treatments in animal models,” he explains, “we may be on the verge of witnessing some remarkable improvements in people with this condition in the not too distant future.”
This issue of M.I.N.D. Matters focuses on two landmark projects that epitomize the best efforts, here or anywhere else in the world, to speed research into treatments and cures for autism and other neurodevelopmental disorders.

The first project, spearheaded by Paul and Randi Hagerman, is the Neurotherapeutics Research Institute (NTRI). This project showcases how our examination of basic science mechanisms and animal models, in this case of fragile X syndrome, can translate to therapeutic applications in a patient-care setting. The Hagermans are international leaders in finding treatments for fragile X and related disorders, using a model approach that we believe will be applicable to many other disorders.

In this issue, we also provide an update on the progress of the Autism Phenome Project (APP), led by David Amaral and Sally Rogers. This comprehensive project utilizes the M.I.N.D. Institute's broad research expertise to understand the complexity of autism. Worldwide, there is nothing like this ambitious and critical project for moving us toward finding effective treatments for this disorder.

Researchers and administrators from a number of prominent research institutions have visited the M.I.N.D. Institute recently. They wanted to learn more about our successful endeavors. How were we able to bring together such a large and diverse group of leading researchers to do collaborative, translational research on neurodevelopmental disorders? Surely, some of our success is due to the proximity of our clinic and our laboratories. It is also related to our pilot research grants program that encourages innovation and collaboration. You will learn more about our recent round of awards for pilot grants in this issue of M.I.N.D. Matters. We fund these pilot grants through the generosity of our donors. These donors make an enormous difference in our ability to test new ideas and encourage researchers to work together to seek treatments and cures for neurodevelopmental disorders.

You'll also learn about David Hessl, one of our younger and already highly successful researchers. While our researchers may vary widely in background and age, they have all come to the M.I.N.D. Institute to collaborate with others who are interested in bringing their varied research skills and knowledge to areas of mutual interest.

Using this model, we have developed and expanded outstanding research programs in multiple critical areas, filling our existing buildings to overflowing. Our research grant support from the National Institutes of Health (NIH) and private foundations has more than doubled in the past three years alone!

As we look forward to the coming year, we are grateful for this generosity and the hope that it offers individuals with neurodevelopmental disorders. We also thank you, our readers, for your generosity and support, and wish you a happy and healthy New Year.

Robert Hendren
Executive Director