



Inside the Institute

Angelman Syndrome Clinic Opens

Exciting Discoveries in Potential Treatment for AS

The new UNC Comprehensive Angelman Syndrome Clinic, funded in part by the Angelman Syndrome Foundation, brings together multiple subspecialists into one setting to address the complex medical and psycho-educational needs of individuals with Angelman syndrome (AS). Through this new clinic, patients and their families have access to a clinical geneticist, neurologist, psychiatrist, psychologist, speech language pathologist, physical/occupational therapist, genetic counselor, social worker and nutritionist, all of whom have expertise in service provision for individuals with developmental disabilities like AS.

During clinic visits, individuals with AS and their families will consult with experts from all subspecialties. Direct assessment will be conducted when appropriate and a treatment/intervention plan will be developed. Collaboration and direct consultation with primary care physicians and other allied health professionals in the patient's medical home will be conducted when needed to assist in streamlining

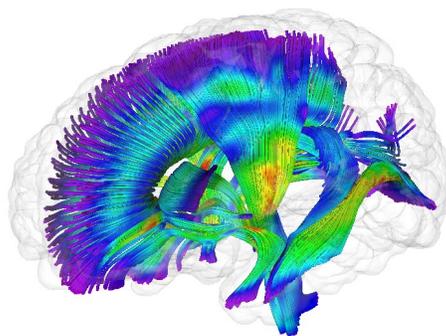
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Differences in Brain Development Evident at 6 Months in Infants Who Develop Autism



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A new study led by CIDD researchers found significant differences in brain development starting at age 6 months in high-risk infants who later develop autism, compared to high-risk infants who did not develop autism. The study, [Differences in White Matter Fiber Tract Development Present From 6 to 24 Months in Infants With Autism](#), is published in the American Journal of Psychiatry. Its results are the latest from the ongoing Infant Brain Imaging Study (IBIS) Network, which is funded by the National Institutes of Health and headquartered at UNC.

The first year of life is a pivotal time for both brain changes and symptom onset in infants later diagnosed with autism spectrum disorders (ASDs). Findings from prospective studies of infant siblings of children with ASDs, who are at higher than average risk for the disorder, indicate that a number of the defining behavioral features of ASDs first emerge around 12 months of age after a period of relatively typical development. Brain changes during this period may have an important role in the pathogenesis of autistic behavior.

Dr. Rebecca Edmondson Pretzel Selected by CDC as an Act Early Ambassador



Rebecca Edmondson Pretzel, Ph.D., has been selected to serve as an Act Early Ambassador for the Centers for Disease Control and Prevention's (CDC's) "Learn the Signs. Act Early." program. Dr. Pretzel will play an important role in educating parents, healthcare professionals, and early educators in North Carolina about early childhood development, warning signs of autism and other developmental disabilities, and the importance of acting early on concerns about a child's development.

Dr. Pretzel was selected as an Act Early Ambassador because of her commitment to improving the lives of children and families and increasing access to services for children with developmental disabilities. Dr. Pretzel's primary clinical and research activities are focused on the screening, assessment, and treatment of young children with or at risk for developmental delays/disabilities, including autism spectrum disorder (ASD), and their families. Her clinical teaching efforts focus on educating graduate students, parents, and interdisciplinary groups of early interventionists on the identification and assessment of developmental delays/disorders in early childhood. Dr. Pretzel has particular areas of expertise and interests that include working with young children who have ASD, intellectual disabilities, and low incidence or complex developmental disabilities.

Developmental disabilities are common in the United States. A recent study shows that about 1 in 6 children has been diagnosed with a developmental disability. It's important that these children are identified early and that they and their families receive the services and support they need.

The Act Early Ambassadors project is designed to develop a network of state-level experts to improve early identification of developmental delay and disability. It is a collaborative project of CDC's National Center on Birth Defects and Developmental Disabilities (NCBDDD), the Health Resources and Services Administration's (HRSA's) Maternal and Child Health Bureau (MCHB), and the Association of University Centers on Disabilities (AUCD).

For more information visit: www.aucd.org/actearly or contact Dr. Pretzel at becky.edmondson@cidd.unc.edu.

The Centers for Disease Control and Prevention's National Center on Birth Defects and Developmental Disabilities, in collaboration with national partners, created a public awareness campaign called "Learn the Signs. Act Early." The campaign aims to educate parents about childhood development, including early warning signs of autism and other developmental disorders, and encourages developmental screening and intervention.

LEND Training Increases Diversity with Self-Advocate Trainee

The goal of LEND (Leadership Education in Neurodevelopmental and Related Disabilities) is to prepare trainees from diverse professional disciplines to assume leadership roles in their respective fields and to improve quality of life for individuals with developmental disabilities and their families. For the second year, LEND recruited a trainee with an intellectual/developmental disability as a self-advocate trainee. This is not a separate program, but an inclusive opportunity that benefits all trainees. Inclusive postsecondary education options have expanded for students with I/DD but this is the only graduate-level opportunity in the nation.



As part of the UNC LEND program trainees engage in learning experiences with a cohort of interdisciplinary trainees including graduate students, faculty, community members, and parents of children with developmental disabilities to build skills and knowledge that prepare them to work in this area. These learning experiences include a weekly course about developmental disabilities, a leadership skill building program, and participation in faculty-led projects. An educational coach offers support to the self-advocate trainee as needed for academic activities. In addition, each LEND trainee works with a faculty mentor to develop personal and professional skills. The training program fosters growth in critical thinking, communication, leadership, professionalism, evidence based practice, advocacy, policy, and research. This opportunity is funded by the Maternal and Child Health Bureau.

Congratulations to Kerry Hagner completed the LEND Self-Advocate Trainee for the 2011-2012 school year. Ms. Hagner is a global messenger for Special Olympics and represented North Carolina in the 2007 World Summer Games in Shanghai, China in cycling. She was employed at Carol Woods Retirement Center in Chapel Hill for seven years, and currently volunteers once a week at the UNC Child Care Center assisting teachers and helping with the children. She is an active member of the NC Postsecondary Education Alliance and represented the CIDD at the PSE Capacity Building Institute in March.

To learn more about LEND Self-Advocate Trainee opportunity contact Deborah Zuver Deborah.Zuver@cidd.unc.edu.



From the Desk of the Director

On October 26, 2011 members of the Carolina Institute gathered for a day long retreat at the Rizzo Center to move forward in developing a strategic plan to guide the institute in the future.



Renee Clark

While on the surface the prospect of a day long retreat to work on a strategic plan doesn't sound like the way most folks would chose to have a good time, I think this retreat actually was enjoyed by most of those that attended. Even more importantly, I think we all came away with the sense that this was the start of an important and necessary process.

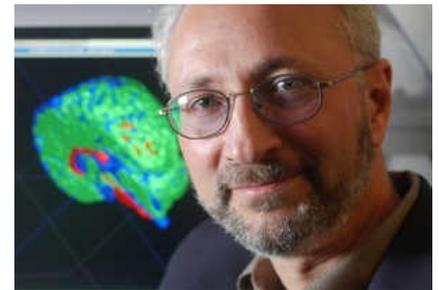


Joe Piven and Portia McCoy

One of the highpoints of the day was the presentations by Dr. Mark Zylka (basic scientist in the Department of Molecular Physiology); Dr. Anne Wheeler (psychologist and Director of the new CIDD Angelman Syndrome Clinic) and Dr. Portia McCoy

(post-doctoral researcher in Dr. Ben Philpot's lab) regarding their individual work with Angelman Syndrome. Mark opened with a review of the research he is conducting along with Ben Philpot and Bryan Roth identifying compounds in a mouse model of Angelman Syndrome for treatment of the underlying genetic defect (methylation of the Ube3a gene) causing the disorder. A subset of individuals affected with Angelman Syndrome meet criteria for autism and thus this targeted treatment has potential relevance for autism. (see the story on this work recently published by Drs. Philpot, Zylka and Roth in Nature on page 1). This brief scientific presentation was followed by a review by Dr. Anne Wheeler of plans for establishing the first clinic in the U.S. specializing in assessment and treatment of individuals with Angelman Syndrome. Dr. Wheeler and her multidisciplinary team of clinicians were recently awarded with the first-ever grant by the [Angelman Syndrome Foundation](#) to support this clinical undertaking and began seeing patients earlier this month. Finally, Portia McCoy took the micro-

phone and relayed her heart-felt experiences as both a researcher and mother attending the annual national meeting of the Angelman Syndrome Foundation. This meeting is an interesting blend of



By Joe Piven, M.D.

families seeking information about the latest research and both clinicians and researchers presenting and exchanging the findings from research and best clinical practices. Portia's description of her first observations of a young boy with Angelman Syndrome and her efforts to project her own views as a mother on to experience of this boy's parents provided a compelling picture of why we were all there that day. Bringing together both basic and clinical research, state-of-the-art multidisciplinary clinical services and cutting-edge clinical and research training relevant to developmental disabilities is a key goal of the strategic plan. This wonderful example made it easy for us to see the importance of our efforts to refining the language of our mission, core values and key objectives. These efforts will be critical in guiding our work together in the coming years.

Following the meeting we had a beautiful lunch together in an intimate room of the old Dubose House at the Rizzo Center. Many thanks to several folks that had a key role in organizing the day – Julia Tarr and Jeff Low for seeing to most of the details of the day, and Maggie Ellis Chotas and Betsy Polk Joseph from [Mulberry Partners](#), outside consultants who were the facilitators and planners of the meeting. And many thanks to all those CIDD faculty, staff and investigators that attended. In the end, what could have been "a very tedious experience had by all" turned out to be an productive and uplifting example of why we are all working together in this field.



CIDD Faculty and LEND Students Host National Conference on Early Identification and Management of Hearing Loss



Over 400 attendees from across the US gathered in Raleigh, NC, October 26-28, for "EHDI: Partnering for Progress." EHDI, an acronym for early hearing detection and intervention, refers to the broad spectrum of systems and services needed to enable newborn hearing screening, diagnosis, and treatment for congenital and early onset hearing loss. Hosted by UNC and developed in cooperation with the National Center for Hearing Assessment and Management (NCHAM) at Utah State University with support from the US Maternal and Child Health Bureau, the meeting combined three conferences: UNC's fifth "Biennial Pediatric Audiology Symposium," the sixth annual "Investing in Family Support Conference," sponsored by NCHAM, and the fourth annual "Southeastern EHDI Conference," sponsored by eight south-

eastern public health programs. Those in attendance included professionals and parent leaders from across the US and nearly 100 graduate students from 14 states and the District of Columbia. Many of the student participants were LEND trainees who received travel grants from AUCD; others had funding from their universities or other sources. According to planning committee chair and CIDD faculty member, Dr. Jack Roush, "combining the conferences enhanced all three meetings while providing valuable opportunities for interdisciplinary interaction and networking." Six plenary sessions featured nationally recognized experts in audiology, early intervention, public policy, medicine, and research, on a variety of issues vital to the EHDI process. Concurrent presentations on specialized topics allowed each conference to retain its individual identity. The meeting was the first of its kind in North Carolina to bring together the full spectrum of EHDI stakeholders and organizations in a single venue. NCHAM director Karl White noted: "The synergy and excitement created by bringing together audiologists, EHDI program staff, graduate students and families was very valuable. Participants left the meeting with great ideas, as well as new partners to help in implementing those ideas!"



LEND trainees from universities across the US traveled to North Carolina, October 26-28, 2011, to participate in *EHDI: Partnering for Progress*

LEND Regional Consortia: Marching Forward Toward Better Systems-of-Care for Everyone

The fundamental goal of the Leadership Education in Neurodevelopmental and Related Disabilities (LEND) training program is to improve the health of infants, children, and adolescents with disabilities. While each LEND Program is unique, shaped in large part by their state and regional needs, the LEND programs are in an important position to provide linkages not only within their respective states, but also to assert a positive impact within their national regions. These collaborative efforts within regions permit the examination of national issues of importance for children with special health care needs and their families, and allow for the sharing of innovative, evidence-based practices and products. Collectively, with technical assistance from the Association of University Centers on Disabilities (www.aucd.org), the LEND programs form a national network that shares information and resources to maximize their impact, with much of the network being organized via regional consortiums. Within the LEND network, there are seven different groups that have organized to address key issues related to their region. Specific regional groups and their LEND (and University Centers for Excellence in Developmental Disabilities) members include:

- PacWest (OR, CA, HI, UT, NM, CO, NV, AK, AZ)
- Southeast Region Consortium (NC, TN-Vanderbilt, TN-Boling, FL-Miami, VA, AL, MS, GA-CLDD, FL-CIC, SC, GA IHDD, KY, MS)
- Northeast New England (VT, NH, CT, MA-Shriver, MA-ICI, NY-Strong, NY-AECOM, NY-Westchester)
- Midwest (SD, NE, KS, MO, IA)
- Great Lakes (WI, MN, IL, IN)
- Mid-Atlantic (DC, MD, VA, WVU, PA-CHOP)
- Central Conference Training Consortium (TN-Boling, TN-Vanderbilt, IN-Riley, OH-Cincinnati, OH-Nisonger, MO, IL, MN, WI, ND, IN-Institute of Disability & Community, KY, MI)

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The North Carolina Autism Alliance

The North Carolina Autism Alliance builds upon, and leverages, existing resources and infrastructure at the North Carolina Leadership Education in Neurodevelopmental and Related Disabilities (NC-LEND), the University Centers for Excellence in Developmental Disabilities Education, Research, and Service (UCEDD), and the Carolina Institute for Developmental Disabilities (CIDD) to address strategic statewide needs in the area of Autism Spectrum Disorders (ASD), and to establish clear goals, objectives, and collaborative action plans associated with these needs. These goals and objectives include infrastructure building for both clinical services and clinical training, and orchestration of advocacy efforts for individuals with ASD and their families.

The composition of the Autism Alliance is diverse and represents a wide range of public and private agencies and organizations (see side bar), as well as consumers, and parents of individuals with ASD. Under the leadership of Chairperson Dr. Stephen Hooper, key objectives of the Alliance include (1) the development of a coordinated system-of-care that is accessible by all consumers with ASD, and their families that extends across the lifespan, and that reduces the time from initial parental concerns to initial service provision; (2) the development of a strong interdisciplinary workforce in the state that is competent with early screening, differential diagnosis, evidence-based interventions, transitional services, and other life skill needs; and (3) targeted emergent selective needs of the state pertaining to ASD.

Initial focus of the Alliance has been on connecting and enhancing an early intervention system of care. Outcomes include the development of NC Part C Early Intervention Service Guidelines for Infants and Toddlers with ASD, statewide training on evidence based practice for early identification of ASD, and a pilot study of Medical Management/Communication among Providers. Sustainable website possibilities have also been explored including the development of a calendar of statewide ASD training activities. This calendar will provide a mechanism for coordinating various trainings across the state in a more systematic fashion so as to maximize training resources for both facilitators and participants. Meetings of the North Carolina Autism Alliance occur on a quarterly basis. For more information about or to join the Autism Alliance, contact Dr. Stephen Hooper, Chairperson, at (919) 966-4808 or Stephen.hooper@cidd.unc.edu.

Agencies involved in the Alliance

• University Representatives

- ◇ Carolina Institute for Developmental Disabilities (LEND, UCEDD, IDDRC)
- ◇ Treatment and Education of Autistic and Communication Related Handicapped Children (TEACCH)
- ◇ School of Public Health
- ◇ Family Support Network
- ◇ Program in Early Autism, Research, Leadership, and Service (PEARLS)
- ◇ School of Public Health
- ◇ Frank Porter Graham Child Development Institute- Professional Development Center
- ◇ UNC Interdisciplinary Graduate Students

• Division of Public Health

- ◇ Early Intervention Branch
- ◇ Children and Youth Branch
- ◇ Genetics & Newborn Screening

• Vocational Rehabilitation

- Department of Public Instruction
- Office of Disability & Health
- Academy of Family Physicians
- Department of Medical Assistance
- Department of Insurance
- Division Mental Health/Developmental Disabilities/ Substance Abuse Services
- Autism Society of North Carolina
- Easter Seals UPC
- Pediatric Society of North Carolina
- Developmental Disabilities Council of North Carolina
- Disability Rights of North Carolina
- Parent Representatives
- Consumers
- NC Commission of Children with Special Health Care Needs



Our Fragile X World—*Currently enrolling families with FXS*

Our Fragile X World is an international community of families and researchers dedicated to providing practical information about the world of fragile X. Through Internet and telephone based surveys, researchers at Our Fragile X World are gathering information about the needs and experiences of thousands of families from around the world who are affected by fragile X syndrome (FXS).

In 2007, more than 1,200 families in the U.S. responded to the first National Fragile X Survey. This survey provided new knowledge about Fragile X and proved that parents are a valuable source of information. More information is needed to understand fragile X better, identify effective treatments, and help meet family needs.

Our Fragile X World was developed through a partnership with RTI International (a non-profit research institute in Research Triangle Park, NC) and CIDD. CIDD researchers involved in the project include Dr. Anne Wheeler, Assistant Clinical Professor in the Department of Psychiatry at UNC, Kristin Cooley, graduate student in UNC's School of Psychology, and Erin Richard, graduate student in the Division of Speech and Hearing Sciences at UNC. RTI International researchers include Don Bailey, Ph.D., Distinguished Fellow at RTI International; Melissa Raspa, Ph.D., Murrey G. Olmsted, Ph.D., and Anne Edwards, B.S. Through this partnership with RTI International, CIDD is working to expand knowledge about the nature and consequences of fragile X syndrome, both for affected individuals and their families, and use this information to inform clinical science, support policy development, and improve professional practice.

Our Fragile X World is currently enrolling families. If you are a biological, step, adoptive, or foster parent of a child (of any age) with fragile X syndrome (either carrier/permutation or full mutation), you are invited to participate in Our Fragile X World. The project also welcomes other family members (e.g., grandparents) who have legal custody of a child with fragile X, as well as family members who are legal guardians of adult family members (e.g., adult sibling). Individuals who do not have any children with fragile X or do not have any children at all can enroll if they or their spouse is a carrier of fragile X or has the full mutation. This also includes individuals who are not married and do not have any children.

Once enrolled, families will be given opportunities to participate in voluntary, confidential surveys about their experiences with fragile X. These surveys will focus on topics such as adults with fragile X, success of new treatments, challenging behaviors, healthcare coverage, and policy needs to better support families.

For more information or to enroll in Our Fragile X World, visit www.ourfragileworld.org or contact Melissa Raspa, Ph.D. 1-866-214-2044; fragilex@rti.org

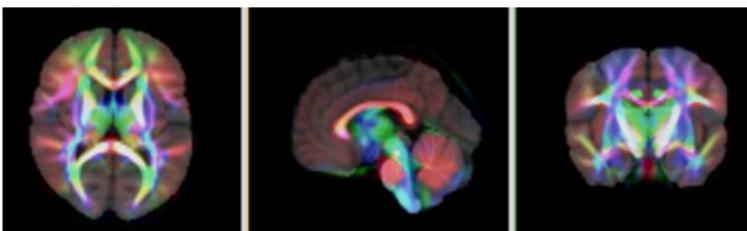


Differences in Brain Development Evident at 6 Months continued

In this study, 92 high-risk infant siblings of older children with ASDs were followed from 6 to 24 months of age. Researchers examined white matter fiber tract organization -- pathways that connect brain regions -- at 6, 12, and 24 months. All 92 participants had diffusion tensor imaging at 6 months and behavioral assessments at 24 months. Most also had additional brain imaging scans at 12 and/or 24 months.

At 24 months, 28 infants met criteria for ASDs and 64 infants did not. The two groups differed in white matter fiber tract development as measured by fractional anisotropy (FA). FA measures the strength and organization of white matter connections, and is based on the movement of water molecules through brain tissue. The FA trajectories for 12 of the 15 fiber tracts examined differed significantly between the infants who developed ASDs versus those infants who did not. Infants who later developed ASDs had higher FA at 6 months, followed by slower change over time relative to infants without ASDs.

"We have a ways to go before a clinically useful biomarker is available. However, these findings hold a great deal of promise for really changing what we mean by early identification and early intervention," says Jason J. Wolff, PhD, lead author of the study and a postdoctoral fellow at the Carolina Institute for Developmental Disabilities (CIDD). "Because infancy is a unique time in terms of brain development, it offers what may be an ideal opportunity for truly effective and even preventative intervention. Though we're not there yet, we may one day be able to advantageously alter an infant's trajectory before autistic symptoms fully manifest and become entrenched. "



Guidelines for Early Intervention Services for Infants and Toddlers

North Carolina's Infant Toddler Program (ITP) provides supports and services statewide for families and their children birth to three years of age who have, or are at established risk for developmental disabilities or delay. The program serves infants, toddlers, and their families who are referred by community resources or self-referred. When a family, pediatrician, community provider, or child care teacher questions whether a child has a developmental disability, the family often needs information, guidance, and support. Both formal and informal supports are critically important to families, and include early intervention services that may be provided. The early intervention system of services is provided under the Individuals with Disabilities Education Act (IDEA). Part C of the IDEA provides the federal mandate for services for young children with special needs, age birth to three years.

This past year, CIDD faculty members have partnered with the NC ITP to produce guidelines for working with children who have specific disabilities. Rebecca Edmondson Pretzel, Ph.D., and Lauren Turner Brown, Ph.D., are part of the team that recently developed the North Carolina Guidelines for Part C Early Intervention Services for Infants and Toddlers with Autism along with Deborah Carroll, Ph.D., Marcia Mandel, Ph.D., Angela Deal, ACSW, and Harriet Bailey, MHA, from the Early Intervention Branch, Women's and Children's Health Section, Division of Public Health. Additionally, Dr. Pretzel and Jean Mankowski, Ph.D. are currently involved with Dr. Carroll in the development of a second guideline: Guidelines for Part C Early Intervention Services for Infants and Toddlers who are Deaf or Hard of Hearing.



The purpose of these sets of Guidelines is to assist staff of the ITP Children's Developmental Services Agencies (CDSAs), providers, and families in better understanding and designing quality evidence-based interventions for those children who are suspected of having autism or who are diagnosed with autism and for children who are deaf or hard of hearing. CDSAs across North Carolina work with local service providers to help families help their children succeed. These Guidelines provide information and guidance on best and/or emerging practices.

Infants and toddlers who are at high risk for significant developmental problems or who have identified disabilities -- such as autism or hearing loss -- benefit from early intervention, as do their families. Research shows that early identification and intervention is critical and offers a window of opportunity to make a positive difference in how a child develops and learns. The goal of the Infant Toddler Program is to support the infant or toddler's development with strategies that can occur within natural learning opportunities and settings and support the family and other caregivers in their pivotal role in caring for and teaching the child. Evidence-based strategies are critical to assuring that the outcomes for the child are met. The Guidelines are available at www.bearly.org.

LEND Regional Consortiums continued

The North Carolina LEND Program, directed by Stephen R. Hooper, Ph.D., Professor of Psychiatry, Psychology, Pediatrics, and Education and Director of Training and Education for the CIDD, has been actively involved in the Southeast Region Consortium. With Dr. Hooper as the Chairperson, this regional group has worked collectively over the past 8 years to develop training activities broadly addressing Title V needs. The group convenes via regular quarterly conference calls, and over the past year has inventoried each program to compile all of their respective training topics and modules. In this regard, the group has a library of over 125 prepared presentations in the areas of Children with Special Health Care Needs, Autism Spectrum Disorders and related Intellectual/Developmental Disabilities, health care services, leadership training, and cultural diversity to mention just a few. Additional initiatives have culminated in an annual training calendar that will showcase each LEND/UCEDD program in the region and, in partnership with AUCD, the training modules will be presented on a monthly basis to a national audience. The "Southeast Region Consortium and AUCD Presents!" program had its inaugural webinar on November of 2011 and will be available to both regional and national audiences.

To learn more about the LEND Regional Consortiums contact:
Dr. Stephen Hooper at (919) 966-5171 or stephen.hooper@cidd.unc.edu.

Angelman Syndrome Clinic Opens continued

services. In addition to these interdisciplinary services, the clinic will provide a foundation for clinical research collaboration and training opportunities for the next generation of clinicians and researchers in the field of neurodevelopmental disabilities. Visit our website at <http://www.cidd.unc.edu/Angelman-Syndrome/> or contact Christie Turcott at (919) 966-2074 for more information.

Eileen Braun is Executive Director of the Angelman Syndrome Foundation whose mission is to advance the awareness and treatment of AS through education, information, research and support for individuals with AS, their families, and other concerned parties. "We are the largest non-governmental funder of Angelman syndrome specific research. Our partnership with UNC and CIDD is an excellent opportunity for us to serve our families in a very direct manner," says Braun. "This comprehensive clinic provides our families with the opportunity to meet the many needs of their individual with Angelman syndrome in one setting and one set of comprehensive exams, without having to visit an array of specialists across different locations and over multiple visits."

Angelman syndrome is a neuro-genetic disorder related to autism that occurs in approximately one in 15,000 newborn children. It is characterized by developmental delay, speech impairment, severe intellectual disability, microcephaly, seizures, movement disorder and a happy demeanor with frequent laughter. Other symptoms may include feeding and swallowing problems, sleep disturb-

ance, hyperactivity, frequent drooling, mouthing behaviors, strabismus, hypopigmentation, scoliosis and constipation. Researchers at UNC have recently identified a compound that shows potential for restoring proper function to the gene that causes AS, representing a possible therapeutic approach for treating the disorder.

AS is caused by the loss or mutation of a single gene - the maternally-inherited copy of the UBE3A gene. While most genes have a functional maternal and a functional paternal copy, UBE3A is relatively unique in that only the maternal copy is expressed in neurons, while the paternal allele lies dormant. This suggests that the neural and behavioral deficits associated with AS could be treated by unsilencing the intact, but dormant, paternal copy of UBE3A. A collaborative effort between Ben Philpot's lab, which has expertise in AS, Mark Zylka's lab, which has expertise in genetics and drug delivery, and Bryan Roth's lab, which has expertise in high-throughput drug screening and analysis, led to the discovery that a group of anti-cancer drugs known as topoisomerase I inhibitors can effectively unsilence the paternal allele of UBE3A. The study, *Topoisomerase inhibitors unsilence the dormant allele of Ube3a in neurons*, was recently published in the journal [*Nature*](#).

"This is the first demonstration that a small molecule approach can be used to unsilence an imprinted, disease-relevant gene," says Philpot. "This has the potential to translate into the first ever therapy for AS, either directly or through the knowledge we gain through our effective compounds. These studies also demonstrate a completely new role, and potential application, of an existing class of FDA-approved compounds."

AS Clinic Opening Celebration



Families, clinicians, UNC colleagues, and members of the Angelman Syndrome Foundation came to celebrate the opening of the clinic on February, 3, 2012.

Click here to watch a video of the program that included presentations by Joe Piven, Ben Philpot, Anne Wheeler, Dr. Charles Williams, Jessica Harvey (Mrs. North Carolina), and Eileen Braun.



Left to Right: Margaret DeRamus, Christie Turcott, Cynthia Powell, Eileen Braun, Eloise Crabb, Robert Christian, Anne Wheeler, Joe Piven, Zheng Fan, Ben Philpot, Charlie Williams

Angelman Syndrome Clinic Opens continued



“We have recently received funding from NIMH and the Angelman Syndrome Foundation to pursue preclinical trials to determine if topotecan can be used in clinical trials for humans,” says Philpot.

“Important steps in this process are to determine if we can optimize drug delivery so that we can rescue physiological and behavioral deficits in AS model mice, and to determine the concentrations that would have to be used for a successful clinical trial in humans.”

“We are incredibly excited about Dr. Philpot’s research and his findings. We know that there is more pre-clinical work that needs to be done and that there needs to be more research on topoisomerase inhibitors, but we look forward to being there with Dr. Philpot and our other researchers as this research continues to unfold,” says Braun. “The Angelman Syndrome Foundation is going to continue to fund the brightest, best, most innovative researchers until we reach our goal of a treatment and ultimately curing Angelman Syndrome.”

The Angelman Syndrome Foundation is celebrating its 20th anniversary this year. “One of the things that we are very proud of is the research and the researchers that we fund. We have a scientific advisory committee that is excellent, not only at stewarding the Foundation’s funds for research, but they also go through a very rigorous review process and thoroughly examine the very best researchers, which is why we are funding Dr. Philpot, Dr. Zylka, and Dr. Roth in this project.”

It was through the Foundation’s Scientific Symposium that Dr. Philpot first conceptualized this research and drug discovery project that would identify how to restore proper function to the gene that causes AS. Braun speaks very highly of Dr. Philpot, stating, “His ability to not only connect with the researchers but also to connect with the families has really led us to this point, which speaks to Dr. Philpot’s character and his desire to not just conduct the research, but most importantly to have an impact on our families.”

Although clinical trials are not currently underway, if you are interested in learning more about possible future clinical trials or about our current clinic services, visit the CIDD Angelman Syndrome website <http://www.cidd.unc.edu/Angelman-Syndrome/>. Other information on Angelman Syndrome in general and on other services and research is available through the Angelman Syndrome Foundation (www.angelman.org).



New NIMH Grant to CIDD Investigators to Study Repetitive Behaviors in Autism

CIDD Associate Director Dr. James Bodfish and CIDD investigator Dr. Gabriel Dichter have been awarded a 5-year grant from NIMH to continue their program of research investigating restricted repetitive behaviors and interests in autism. The project will focus on a distinct subtype of repetitive behaviors called circumscribed interests. Circumscribed interests are nearly universal in autism, are clinically impairing, and are characterized by intense focus on a narrow range of subject areas and by the rigid organization of activities exclusively around these interests (e.g., collecting, manipulating, excessive question-asking, etc). This research will examine the neurobiology of circumscribed interests by linking behavioral manifestations of symptoms with measures derived from functional magnetic resonance imaging (fMRI), affect-modulated psychophysiology, and eyetracking approaches with a particular focus on the functional integrity of brain reward circuitry. By contrasting neurobiological and behavioral profiles in adolescents with autism (both low and high functioning) with adolescents with obsessive compulsive disorders and with typical development, Drs. Bodfish and Dichter are aiming to determine which types of repetitive behaviors are clinically significant and unique in autism. Answering these questions would refine diagnostic practice, would focus the search for specific genetic, neurobiologic, and cognitive mechanisms of autism, and would ultimately direct the development of novel forms of treatment for autism. This investigation will leverage collaborations with Dr. John March, Director of the Division of Neurosciences Medicine at the Duke Clinical Research Institute, Dr. Noah Sasson, Assistant Professor in the School of Behavioral and Brain Sciences at UT-Dallas and former CIDD T32 trainee, and Dr. Lauren Turner-Brown, a CIDD investigator. These research efforts will also dovetail with a number of student projects, including the dissertation projects of Cara Damiano (supported by an Autism Speaks Weatherstone Predoctoral Fellowship) in the Clinical Psychology program and Anna Sabatino in the Developmental Psychology Program, as well as the undergraduate psychology honors thesis projects of Joey Aloï and Ryan Delapp.

CIDD Trainee Accomplishments and News

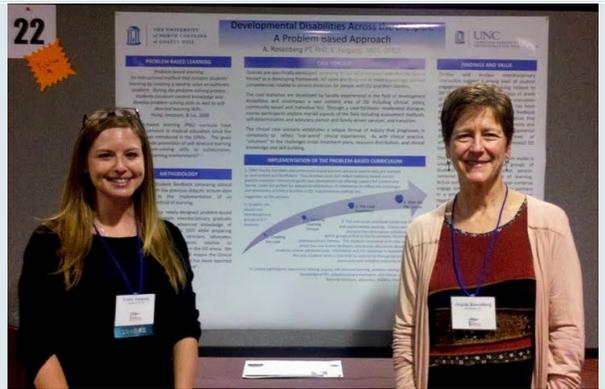
New Trainee Liaison: Congratulations to **Megan Kovac**, CIDD's newest Leadership Education in Neurodevelopmental Disorders (LEND) Trainee Liaison. Megan is a third-year doctoral student in the School Psychology program at UNC, and a second year LEND trainee in Special Education. LEND Trainees at the CIDD are also part of the Association of University Centers on Disabilities (AUCD). AUCD is a national network of interdisciplinary institutions, like the CIDD, that are dedicated to research, advocacy, and service in the field of developmental disabilities. This network is a tremendous resource, offering everything from policy briefs to Disability Practice Toolkits.



In order to ensure that trainees at the CIDD are aware of and connected to the broader AUCD network, Megan will work with the Virtual Trainee (Jody Pirtle at the University of Arizona) to promote awareness of AUCD news, events, and resources. Additionally, the Trainee Liaison hopes to promote the activities and achievements of trainees at the CIDD.

Trainees, if you haven't already, please visit the AUCD Trainee Webpage on the AUCD website (<http://www.aucd.org>), the AUCD Trainee Facebook page (<http://www.facebook.com/pages/AUCD-Trainees/91722974878>), or subscribe to the Trainee Listserve. The Trainee Facebook page is updated every day with news and events at AUCD institutions. "These resources are great for staying informed about policy, professional development, funding opportunities, and for staying inspired to do the work that we do!" says Megan. "I am a huge believer in the multidisciplinary approach of the CIDD, and I love being part of a place that values collaboration throughout research, advocacy, and clinical service."

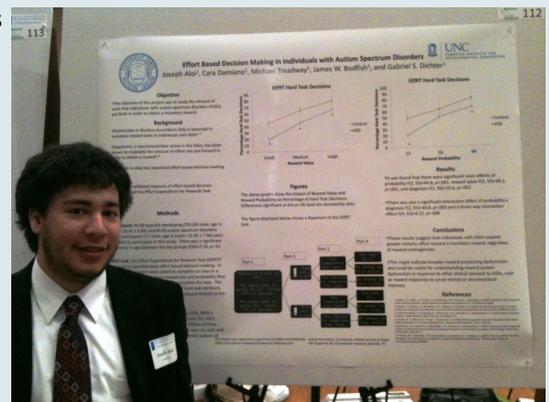
AUCD Annual Conference Scholarship: Congratulations to **Emily Furgang**, OT LEND trainee who was awarded the AUCD Annual Conference Travel Scholarship and presented a poster with Dr. Angela Rosenberg entitled "DD Across the Lifespan: An Interdisciplinary Approach (Problem-based curriculum)". The purpose of this poster was to communicate the CIDD's unique educational opportunity for LEND trainees. It discussed the faculty-mentored, problem-based learning course in which LEND trainees, as well as students from across the university, learn about developmental disabilities across the lifespan. The poster displayed a model for this curriculum, including methodology, implementation, and preliminary findings.



Physical Therapy Collaboration: 2011-2012 marked the initiation of a unique collaborative experience offered by The University of North Carolina and Duke University. The UNC Carolina Institute for Developmental Disabilities LEND fellowship and the Duke Department of Physical Therapy and Occupational Therapy Pediatric residency joined together to offer a unique opportunity to the pediatric physical therapy community. The goal of this collaborative effort is to offer a comprehensive and interdisciplinary experience in clinical management and leadership throughout the physical therapy continuum in the specialty area of pediatrics and developmental disabilities. **Kimberly Morgan**, PT, DPT served as the 2011-2012 University of North Carolina CIDD Physical Therapy LEND Fellow and the Duke Pediatric Physical Therapy Resident. She has been mentored at UNC by Angela Rosenberg, PT, Dr.P.H. and Kathleen Ollendick, PT, DPT, PCS.



Honors Theses Completed: **Joey Aloj**, a UNC senior, completed his honor's thesis in Dr. Gabriel Dichter's lab. The title of Joey's thesis was "Effort-Based Decision Making in Individuals with Autism Spectrum Disorders," and the data collected for this project have been submitted for publication to the Journal of Neurodevelopmental Disorders. Co-authors on the study were Carolina Institute for Developmental Disabilities Associate Director Dr. James W. Bodfish, Cara Damiano, and Michael Treadway of Vanderbilt University. The photo is from the UNC Celebration of Undergraduate Research, held on April 16th, 2012. **Ryan Delapp** also completed an honors thesis in Dr. Gabriel Dichter's lab on the effects of aripiprazole on patterns of brain activation in autism, and both Joey and Ryan received highest honors for their projects. Congratulations, Joey and Ryan!



Announcements:

- CIDD Director, Dr. Joe Piven, was recently invited to Washington, D.C. at the request of Senator Sherrod Brown's office (D, Ohio) to participate in a discussion of "Root Causes of the Autism Epidemic". NIMH Director, Tom Insel, Senator Brown and his staff, and three other researchers in the field attended the meeting which was held in the Senate Visitor's Center of the Capitol Building. Dr. Piven presented findings from the work of the NIH funded Autism Center of Excellence Network he directs on imaging infants at risk for autism; as well as the results of a national conference convened last year to propose a national research agenda for studying autism in elderly individuals. The former research informs the field about the onset and origins of autism. The latter has important implications for the current high prevalence rates of autism reported.

Recently Published Papers:

- ⇒ "Angelman syndrome: insights into genomic imprinting and neurodevelopmental phenotypes" published in *Trends in Neurosciences* provides a comprehensive overview of Angelman syndrome, which occurs in 1 out of every 12,000 births. The manuscript authored by Angela Mabb, Matthew Judson, Mark Zylka, and Ben Philpot encompasses the most recent advances in Angelman syndrome from a biological and physiological perspective. Further, the authors propose future studies that may allow researchers to gain a better understanding of this debilitating neurodevelopmental disorder.
- ⇒ One of the major obstacles in autism research is the absence of valid animal models that fully recapitulate the behavioral features of autism. Recent work has identified mutations in *SHANK3* gene in some autism-spectrum disorder (ASD) patients. In collaboration with the Philpot Lab at UNC, researchers at Duke University Medical School have mutated two of the major splice variants of *Shank3* found in the mouse brain and report that these mutant mice display behaviors that are very similar to those of ASD patients. The study "Synaptic dysfunction and abnormal behaviors in mice lacking major isoforms of Shank3" was recently published in the journal *Human Molecular Genetics*.

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THE CIDD AND TEACCH COLLABORATE TO
CELEBRATE AUTISM AWARENESS DAY 2012

