



*BABY SIBLINGS
RESEARCH CONSORTIUM
2010 ANNUAL REPORT*



AUTISM SPEAKS™

www.AutismSpeaks.org

Executive Summary

1. The Committee of Principal Investigators of the BSRC now includes 25 members, representing 21 different research programs.
2. Around 3000 infants at risk for ASD have enrolled thus far in BSRC projects; in the coming year we expect to enroll more than 800 additional high risk infants.
3. In 2010, 35 papers were published in peer-review journals on topics directly relevant to the mission of the BSRC. One paper, by Sally Ozonoff and her colleagues from UC Davis and UCLA was selected as one of 20 “top scientific advances” by the IACC
4. BSRC research programs provided research training to 40 doctoral students and 27 post-doctoral fellows.
5. Eighteen new grants were awarded to members of the BSRC in 2010 to support further research on high risk infants.
6. Work on collaborative projects and network projects is proceeding with the expectation that several will be submitted for publication in the coming year.
7. This year the MOA for the BSRC was revised and approved by all members. Additions to the MOA included a set of common measures expected from all member groups and criteria for associate membership were defined and approved.
8. The BSRC submitted a grant application to AS to secure funding for the BSRC database. This grant was awarded for 2 years.



An enthusiastic participant in a BSRC research study. Photo courtesy of Wendy Stone



A child helps to uncover clues to earlier detection of ASD. Photo courtesy of Cathy Lord

Baby Sibling Research Consortium (BSRC) - Mission

The BSRC focuses on investigations of infants at risk for autism spectrum disorders (ASD) using a variety of methods, including behavioral and neurobiological measures. The organization respects the integrity of the individual researchers and research groups while at the same time creating a framework for collaborative research activities (with new or existing funding at each site) and data sharing through this new entity. We have agreed to pool our data for collaborative projects, thereby considerably enhancing the prospects of achieving our research goals.



Members of the BSRC



The organization is made up of a Committee of Principal Investigators (CPI) representing major research groups participating in the BSRC. Each member of the BSRC is a PI on a funded project investigating infants/toddlers at risk for ASD.



Committee of Principal Investigators



Susan Bryson, Ph.D.	Dalhousie University, Halifax, Canada
Alice Carter, Ph.D.	University of Massachusetts, Boston
Leslie Carver, Ph.D.	UCSD
Tony Charman, Ph.D.	Institute of London, representative for British Autism Study of Infant Siblings (BASIS)
Kasia Chawarska, Ph.D.	Yale University
John Constantino, M.D.	Washington University
Suzanne Curtin, Ph.D.	University of Calgary
Karen Dobkins, Ph.D.	UCSD
Deborah Fein, Ph.D.	University of Connecticut
Judith Gardner, Ph.D.	Institute of Basic Research
Jana Iverson, Ph.D.	University of Pittsburgh
Ami Klin, Ph.D.	Yale University
Rebecca Landa, Ph.D.	Kennedy Krieger Institute
Catherine Lord, Ph.D.	University of Michigan
Daniel Messinger, Ph.D.	University of Miami
Sally Ozonoff, Ph.D.	MIND Institute, UC Davis
Joseph Piven, M.D.	University of North Carolina
Sally Rogers, Ph.D.	MIND Institute, UC Davis
Marian Sigman, Ph.D.	UCLA
Wendy Stone, Ph.D.	University of Washington/Vanderbilt University
Mark Strauss, Ph.D.	University of Pittsburgh
Helen Tager-Flusberg, Ph.D.	Boston University
Sara Webb, Ph.D.	University of Washington/Seattle Children's Research Institute
Nurit Yirmiya, Ph.D.	Hebrew University, Jerusalem Israel
Lonnie Zwaigenbaum, M.D.	University of Alberta, Edmonton, Canada

Autism Speaks Project Staff

Geraldine Dawson, Ph.D.
Alycia Halladay, Ph.D.
Andy Shih, Ph.D.

NIH Project Staff

NICHD: Alice Kau, Ph.D.



External Advisory Committee

The following individuals serve on the External Advisory Committee for the BSRC:



Heidi Feldman, M.D. (Stanford University)
Alan Fogel, Ph.D. (University of Utah)
Nathan Fox, Ph.D. (University of Maryland)
Peter Mundy Ph.D. (UC Davis/MIND Institute) – continuing member
Alison Singer (Autism Science Foundation and parent)
Ezra Susser, M.D. (Columbia University)



BSRC Officers: Executive Committee

The BSRC Executive Committee is responsible for organizing and coordinating all functions of the BSRC. Current officers (for 2009-10) include:

Chair	Sally Ozonoff
Member	Helen Tager-Flusberg
Member	Rebecca Landa
Member	Daniel Messinger



Participants in BSRC Projects

There are currently close to 3000 infants at risk for ASD enrolled and participating in active projects. In addition, about 1200 infants from “low risk” or non-affected families are included in BSRC studies.



Annual Meeting Summary

On January 25 and 26, 2010, members of the BRSC met in San Diego, California for their annual meeting to review the year's research progress and discuss future collaborative directions. This year's meeting continued the group's discussions on regression in infant siblings. Being able to make better predictions about which children will show regression is an urgent question in autism research. However, regression has so far been very difficult to investigate, primarily because most studies up to this point have had no choice but to use retrospective methods (usually parent recall). Studying regression with prospective methods, in which researchers can use objective measures to collect data on development as it is happening, will be a much more powerful approach. Therefore, this year's

symposium on regression compared traditional retrospective methods of measuring regression (e.g., Autism Diagnostic Inventory, or ADI-R) to prospective methods such as the MacArthur-Bates Communicative Development Inventory (CDI) and the Mullen Scales of Early Learning. The researchers also explored novel methods to examine regression, such as direct coding of behaviors like eye contact and using online diaries to capture information. The ultimate goals of this work are to understand 1) how to best measure regression, 2) which children are vulnerable to later regression, and 3) what the earliest warning signs of regression may be.

Later, the consortium broke out into smaller groups to brainstorm and share best practices on two important topics: studying brain function using non-invasive techniques such as EEG and eye tracking, and discussing clinical issues related to early detection, such as sharing information with families and the diagnostic stability of symptoms. These smaller breakout sessions were a new feature of the annual meeting that allowed more focused discussions on topics in order to better shape research, policy, and communication strategies. Attendees were very positive about these breakout groups, which may become a fixture of future BSRC annual meetings.



Some BSRC studies are examining brain function using EEG techniques in infants as young as 12 months old. Photo courtesy of Wendy Stone

The second day of the meeting focused on development of collaborative projects and the resources and infrastructure needed to facilitate such endeavors in the future, such as developing a BSRC database and requiring all studies to administer a set of common measures. It is difficult for any one site to follow enough children to answer many of the critical questions in the field, so collaboration across sites and pooling of information and data is critical to determine best practices in the important areas of early detection, diagnosis and intervention.

Three major findings in high-risk infant research based on published research in 2010

1. **Ozonoff, S., Iosif, A. M., Baguio, F., Cook, I. C., Hill, M. M., Hutman, T., et al. (2010). A Prospective Study of the Emergence of Early Behavioral Signs of Autism. *Journal of the American Academy of Child and Adolescent Psychiatry*. 49(3):256-266.**

No differences in social behavior at 6 months, followed by declining rate of development in children with ASD in the first three years of life. The majority of infants showed a gradual loss of social skills, but the regression was not noticed by most parents. This demonstrates a flaw in retrospective studies on onset using parent report.



Sally Ozonoff from the UC Davis MIND Institute plays with an toddler enrolled in a BSRC study

2. **Bhat, A., Galloway, C., Landa, R.J. (2010) Social and Non-social Visual Attention Patterns and Associative Learning in Infants at risk for Autism. *Journal of Child Psychology and Psychiatry*. 51(9):989-97.**

At 6 months of age, siblings of children with autism (sibs-A) learned the association between moving a switch and activating a cause-effect toy as well as low-ris controls.

However, sibs-A spent less time looking at caregivers and more time looking at the toy or joystick when their caregivers made no attempts to engage their attention. Response to caregiver-initiated social bits was comparable for both groups. Infrequent self-initiated socially directed gaze may be an early marker of later social and communication delays.



The research team studying autism at Kennedy Krieger Institute led by Rebecca Landa

3. Karmel B.Z., Gardner, J.M, Meade, L.S., Cohen, I.L., London, E., Flory M.J, Lennon, E.M., Miroshnickenko I, Rabinowitz, S., Parab, S., Barone A and Harin, A. (2010) Early Medical and Behavioral Characteristics of NICU Infants Later Classified with ASD. Pediatrics, 126:457-467

The authors study children born in the neonatal intensive care unit to identify very early behaviors relating to atypical development. Comparing children diagnosed with ASD vs. those who were not later diagnosed, there were several atypical behaviors that were seen by 4 months of age. These include visual tracking, tone, and regulation.



A premature infant examined for a number of early behaviors

Publications in 2010

This section of the report presents a summary of the papers and book chapters published in 2010 by members of the CPI on topics directly related to their research on infants/toddlers at risk for ASD.

[** Indicates more than one CPI member as co-author]

BASIS

Charman, T. (2010). Autism research comes of (a young) age (Invited Editorial). *Journal of the American Academy of Child and Adolescent Psychiatry* 49: 208-209.

Elsabbagh, M. & Johnson, M.H. (2010). Getting answers from babies about autism. *Trends in Cognitive Science*, 14: 81-87.

Holmboe, K., Elsabbagh, M., Volein, A., Tucker, L.A., Baron-Cohen, S., Bolton, P., Charman, T., & Johnson, M.H. (2010). Frontal cortex functioning in the infant broader autism phenotype. *Infant Behavior & Development*, 33: 482-491.

**Yirmiya, N. & Charman, T. (2010). The prodrome of autism: early behavioral and biological signs, regression, peri- and post-natal development and genetics. *Journal of Child Psychology and Psychiatry*, 51: 432-458.

Susan Bryson, Dalhousie University

Coolican, J., Smith, I., & Bryson, S. E. (2010). Brief parent training in Pivotal Response Treatment for preschoolers with autism. *Journal of Child Psychology and Psychiatry*, 51(12): 1321-1330.

Bryson, S. E. (2010). The early development of visual-spatial attention. In R. E. Tremblay, R. G. Barr, R. D. Peters & M. Boivin (Eds.), [Encyclopedia on Early Childhood Development \[Online\]](#) (pp. 1-6). Montreal, Quebec: Centre of Excellence for Early Childhood Development.

Alice Carter, University of Massachusetts/Boston

Carter, A.S., Wagmiller, R.J., Gray, S. A. O., McCarthy, K.J., Horwitz, S.M., & Briggs-Gowan, M.J., (2010). Prevalence of DSM-IV Disorder in a Representative Healthy Birth Cohort at School Entry: Sociodemographic Risks and Social Adaptation. *Journal of the American Academy of Child and Adolescent Psychiatry*, 49(7): 686-98

Kasia Chawarska, Yale University

Paul, R., & Roth, F. (2010). Characterizing and Predicting Outcomes of Communication Delays in Infants and Toddlers: Implications for Clinical Practice. *Language, Speech, and Hearing Services in Schools*, Nov 24. [Epub ahead of print]

**Charwarska, K., Volkmar F., Klin A. (2010) Limited attentional bias for faces in toddlers with autism spectrum disorders. *Archives of General Psychiatry*, 67(2): 178-185.



The Chawarska Lab at Yale University focuses on early social processing in infants at risk for ASD.

John Constantino, Washington University

Constantino, J.N., Majmudar, P., Bottini, A., Arvin, M., Virkud, Y., Simons, P. & Spitznagel, E. (2010) Infant head growth in male siblings of children with and without autism spectrum disorders. *Journal of Neurodevelopmental Disorders*, 2(1): 39-46.

Constantino, J.N., Zhang, Y., Frazier, T., Abbacchi, A.M. & Law, P. (2010) Sibling recurrence and the genetic epidemiology of autism. *American Journal of Psychiatry*, 167(11): 1349-1356.

Karen Dobkins, University of California at San Diego



Karen Dobkins

Cui Koh H., Milne E. & Dobkins K.R. (2010). Contrast Sensitivity for Motion Detection and Direction Discrimination in Adolescents with Autism Spectrum Disorders and their Siblings. *Neuropsychologia*, 48 (14): 4046-56.

Judy Gardner, NYS Institute for Basic Research

Karmel, B. Z., Gardner, J. M., Meade, L. S., Cohen, I. L., London, E., Flory, M. J., Lennon, E. M., Miroshnichenko, I., Rabinowitz, S., Parab, S., Barone, A., & Harin, A. (2010). Early medical and behavioral characteristics of NICU infants later diagnosed with Autism Spectrum Disorder (ASD). *Pediatrics*, 126, 457-467.

Cohen, I. L., Gomez, T. R., Gonzales, M. G., Lennon, E. M., Karmel, B. Z., & Gardner, J. M. (2010). Parent PDD Behavior Inventory profiles in young children classified according to Autism Diagnostic Observation Schedule-Generic or Autism Diagnostic Interview-Revised Criteria. *Journal of Autism and Developmental Disorders*, 40, 246–254.

Rebecca Landa, Kennedy Krieger Institute/Johns Hopkins University

Bhat, A., Galloway, C., Landa, R.J. (2010). Social and non-social visual attention patterns and associative learning in infants at risk for autism. *Journal of Child Psychology and Psychiatry*. 51(9):989-97.

Kalb, L., Law, K., Landa, R., Law, P. (2010). Onset patterns prior to 36 months in autism spectrum disorders. *Journal of Autism and Developmental Disorders*. 40(11):1389-402.



Cathy Lord

Cathy Lord, University of Michigan

Kim, S., & Lord, C. (2010). Restricted and repetitive behaviors in toddlers and preschoolers with autism spectrum disorders based on the Autism Diagnostic Observation Schedule (ADOS). *Autism Research*, 3(4), 162-173.

Richler, J., Huerta, M., Bishop, S. L., & Lord, C. (2010). Developmental trajectories of restricted and repetitive behaviors and interests in children with autism spectrum disorders. *Development and Psychopathology*, 22(1), 55-69.

Grzadzinski, R., Di Martino, A., Brady, E., Mairena, M.A., O'Neale, M., Petkova, E., Lord, C. & Castellanos, F.,X. (2010). Examining autistic traits in children with ADHD: Does the autism spectrum extend to ADHD? *Journal of Autism and Developmental Disorders*. Nov 25 epub ahead of print.

Daniel Messinger, University of Miami

Haltigan JD, Ekas NV, Seifer R, Messinger DS. (2010). Brief Report: Attachment Security in Infants At-Risk for Autism Spectrum Disorders. *Journal of Autism and Developmental Disorders*. [epub ahead of print]

Baker J. K., Messinger, D.S., Lyons K.K., & Grantz, C.J. (2010). A Pilot Study of Maternal Sensitivity in the Context of Emergent Autism. *Journal of Autism and Developmental Disorders*, 40(8):988-99. .

Baker, J., Haltigan, J.D., Brewster, R., Jaccard, J. & Messinger, D.S. (2010). Non-Expert Ratings of Infant and Parent Emotion: Concordance with Expert Coding and Relevance to Early Autism Risk. *International Journal of Behavioral Development*, 34: 88–95

Chow, S., Haltigan, J.D., Messinger, D.S. (2010). Dynamic Infant-Parent Affect Coupling during the Face-to-Face/Still-Face. *Emotion*, 10: 101-114.



The research team studying autism led by Dr. Sally Ozonoff at the University of California at Davis

Sally Ozonoff, University of California at Davis

**Ozonoff, S., Iosif, A., Baguio, F., Cook, I.C., Hill, M.M., Hutman, T., Rogers, S.J., Rozga, A., Sangha, S., Sigman, M., Steinfeld, M.B., & Young, G.S. (2010). A prospective study of the emergence of early behavioral signs of autism. *Journal of the American Academy of Child and Adolescent Psychiatry*, 49: 258-268.

**Schwichtenberg, A.J., Young, G.S., Sigman, M., Hutman, T., & Ozonoff, S. (2010). Can family affectedness inform infant sibling outcomes of autism spectrum disorders? *Journal of Child Psychology and Psychiatry*, 51: 1021 – 1030.

Christensen, L., Hutman, T., Rozga, A., Young, G.S., Ozonoff, S., & Rogers, S.J. (2010). Play and developmental outcomes in infant siblings of children with autism. *Journal of Autism and Developmental Disorders*, 40: 946-957

Wendy Stone, University of Washington/Vanderbilt University

Noland, J.S., Reznick, J.S., Stone, W.L., Walden, T.A., & Sheridan, E.H. (2010). Differential working memory for social and nonsocial stimuli in infant siblings of children with autism spectrum disorder. *Developmental Science*, 13, 244-251.

Marian Sigman/Ted Hutman, UCLA

Christensen, L., Rozga, A., Hutman, T., Young, G.S., Ozonoff, S., Rogers, S.J., & Sigman, M. (2010) Play Trajectories in Infant Siblings of Children with Autism, *Journal of Autism and Developmental Disabilities*, 40(8): 946-957.

Hutman, T., De Laurentis, A.D., Rozga, A., Barnwell, J.M., Sugar, C., & Sigman, M. (2010) Response to Distress in Infants at Risk for Autism: A Prospective Longitudinal Study, *Journal of Child Psychology & Psychiatry*, 51(9): 1010-1020.

**Ozonoff, S., Iosif, A.-M., Baguio, F., Cook, I.C., Hill, M.M., Hutman, T., Rogers, S.J., Rozga, A., Sangha, S., Sigman, M., Steinfeld, M.B., and Young, G.S. (2010) A Prospective Study of the Emergence of Early Behavioral Signs of Autism, *Journal of the American Academy of Child and Adolescent Psychiatry*, 49(3):208-9.

**Schwichtenberg, A. J., Young, G.S., Sigman, M., Hutman, T., & Ozonoff, S., (2010) Can Family Affectedness Inform Infant Sibling Outcomes of Autism Spectrum Disorders? *Journal of Child Psychology & Psychiatry*, 51(9), 1021-1030.

**Seidman, I., Yirmiya, N., Alon, R., Ben Yitzhak, N., Lord, C., & Sigman, M. (2010). Diagnostic outcomes in school age siblings of children with autism. *International Public Health Journal*, 2, 113-124.

Mark Strauss, University of Pittsburgh

Newell, L. C., Best, C. A., Gastgeb, H., Rump, K. M., & Strauss, M. S. (2010). The development of categorization and facial knowledge: Implications for the study of autism. In L. M. Oakes, C. H. Cashon, M. Casasola & R. H. Rakison (Eds.), The information processing infant. New York: Oxford Press.

Helen Tager-Flusberg, Boston University

Tager-Flusberg, H. (2010). The origins of social impairments in autism spectrum disorder: Studies of infants at risk. *Neural Networks*, 23, 1072-1076.

Sara Jane Webb, University of Washington

Webb, S.J., Jones, E., Merkle, K., Toth, K., Greenson, J., & Dawson, G. (2010). Toddlers with elevated autism symptoms show slowed habituation to faces. *Child Neuropsychology*, 16(3), 255-278

Webb, S.J., Shell, A. R., Cuomo, J., Jensen, G., Deutsch, C. (2010). Head circumference measurement and growth. Applications to Neurodevelopment. In Preedy (Ed.) Handbook of Growth and Growth Monitoring in Health and Disease. Springer.

Nurit Yirmiya, Hebrew University

**Yirmiya, N. & Charman, T. (2010). The prodrome of autism: early behavioral and biological signs, regression, peri- and post-natal development and genetics. *Journal of Child Psychology and Psychiatry*, 51, 432-458.

**Seidman, I., Yirmiya, N., Alon, R., Ben Yitzhak, N., Lord, C., & Sigman, M. (2010). Diagnostic outcomes in school age siblings of children with autism. *International Public Health Journal*, 2, 113-124.

Lonnie Zwaigenbaum, University of Alberta

Zwaigenbaum L. (2010) Advances in the Early Detection of Autism. *Current Opinion in Neurology*. 2, 97-102.

Newly Funded Grants in 2010

BASIS

- ESRC Hill, PI 2010
"The role of motor abilities in the development of typical and atypical social behavior"
- European Science Foundation Charman, PI 2010-2014
"Enhancing the scientific study of early autism (ESSEA) COST action"
- Autistica: McCleery, PI 2010-2012
"Electrophysiological pilot studies of auditory sensory-perceptual processing in toddlers at risk for autism"

Susan Bryson, Dalhousie University

- **CIHR Bryson and Zwaigenbaum (PIs) 2010-2015
"Understanding early developmental trajectories in autism: From infancy to age 8"
- **Autism Speaks Canada Bryson and Zwaigenbaum (PIs) 2010-2013
"Improving early diagnosis and treatment for ASD: The Canadian Infant Sibling Project"
- **NCE: Bryson and Zwaigenbaum (PIs) 2010-2013
"Genomic influences on brain and behavioral trajectories in autism spectrum disorders"

Kasia Chawarska, Yale University

- NIMH: Charwarska, PI 2010-2015
"Development of face processing in infants with ASD"

Karen Dobkins, UCSD

- **NINDS Dobkins, PI and Carver and Schmid-Schonbein (co-PIs) 2010-2014
"Are Autism Spectrum Disorders Associated with Leaky-Gut at an Early Critical Period in Development?"

Rebecca Landa

- NICHHD Caulfield, PI 2010-2011
"Development and Validation of an Autism Case Confirmation Approach for Use in the National Children's Study (Formative Research 8)"

Catherine Lord, University of Michigan

Autism Speaks Lord, PI 2010-2013
“Early social interaction: Community outreach project”

Daniel Messinger, University of Miami

NICHD Lipshultz, PI 2010-2011
“Development and Validation of an Autism Case Confirmation Approach for Use in the National Children’s Study (Project #8)”

NICHD Ekas, PI 2010-2012
“The emergence of emotion regulation in children at risk for autism spectrum disorders”

Wendy Stone, University of Washington

NICHD Faustman, PI 2010-2011
“Development and Validation of an Autism Case Confirmation Approach for Use in the National Children’s Study (Formative Research 8)”

Mark Strauss, University of Pittsburgh

NIMH Contura, PI 2010-2012
“Developmental characteristics of diffusion tensor pathway changes in autism”

NIMH Campbell, PI 2010-2015
“Early social and emotional development in toddlers at genetic risk for autism”

Autism Science Foundation: Hannigen, PI 2010-2011
“Defining high- and low-risk expression of emotion in infants at-risk for autism”

Sara Jane Webb, University of Washington

NICHD Webb, PI 2010-2015
“Physiology of attention and regulation in children with ASD”

Autism Speaks Weatherstone Fellowship Burner, PI 2010-2011
“Observational and electrophysiological assessments of temperament in infants at-risk for ASD”

Lonnie Zwaigenbaum, University of Alberta

**CIHR Bryson and Zwaigenbaum (PIs) 2010-2015

“Understanding early developmental trajectories in autism: From infancy to age 8”

**Autism Speaks Canada Bryson and Zwaigenbaum (PIs) 2010-2013
“Improving early diagnosis and treatment for ASD: The Canadian Infant Sibling Project”

**NCE: Bryson and Zwaigenbaum (PIs) 2010-2013
“Genomic influences on brain and behavioral trajectories in autism spectrum disorders”

Doctoral and Post-Doctoral Training on BSRC Projects

The following graduate students and post-doctoral fellows were actively involved in the research programs directed by members of the CPI that focused on high risk infants.

BASIS

Sam Wass – Doctoral student (IOE London)
Rachel Bedford - Doctoral student (IOE London; Funding)
Wafa Alshami – Doctoral student (IOE London)
Sarah Lloyd Fox – Doctoral student (Birkbeck London)
Sissy Stefanidou – Doctoral student (Birmingham University)
Kate Graham - Doctoral student (Birmingham University)

Mayada Elsabbagh PhD – Postdoctoral Fellow (Birkbeck London)
Teodora Gliga PhD – Postdoctoral Fellow (Birkbeck London)
Jeanne Guiraud PhD- Postdoctoral Fellow (Birkbeck London)
Susie Chandler PhD – Postdoctoral Fellow (IOE London)
Greg Pasco PhD – Postdoctoral Fellow (IOE London)
Anna Blasi PhD – Postdoctoral Fellow (Institute of Psychiatry)

Susan Bryson, Dalhousie

Vickie Armstrong, PhD – Postdoctoral Fellow (Funding: CIHR)

Leslie Carver, UCSD

Katherine Meltzoff – Doctoral student

Suzanne Curtin, University of Calgary

Danielle Droucker -Doctoral student

Kasia Chawarska, Yale University

Tina Goldsmith, PhD. – Postdoctoral fellow
Amanda Steiner, PhD. – Postdoctoral fellow
Fred Shic, PhD. – Postdoctoral fellow

Karen Dobkins, UCSD

Vanitha Sampath Ph.D. - Postdoctoral fellow
Alex Penn PhD. – Postdoctoral fellow

Deborah Fein, University of Connecticut

Katelin Carr – Doctoral student
Alex Hinnebusch, Doctoral student
Laura Brennan, Doctoral student



Deborah Fein

Jana Iverson, University of Pittsburgh

Neena Leezenbaum – Doctoral student
Jessie Northrup – Doctoral student
Meaghan Venezia Parladé – Doctoral student
Eve Sauer LeBarton - Postdoctoral fellow

Rebecca Landa, Kennedy Krieger Institute

Natalie Rallis, - Doctoral student
Joanne Flanagan, – Doctoral student
Alden Gross, Doctoral student

Annie Inge, PhD - Postdoctoral fellow
Klaus Libertus PhD – Postdoctoral fellow

Catherine Lord, University of Michigan

Sophy Kim – Doctoral student
Themba Carr – Doctoral student
Kristina Lopez – Doctoral student
Vanessa Hus – Doctoral student
Kaite Gotham PhD – Postdoctoral fellow

Daniel Messinger, University of Miami

Caroline Grantz, Doctoral student
Nicole McDonald, Doctoral student.
Devon Gangi. Doctoral student

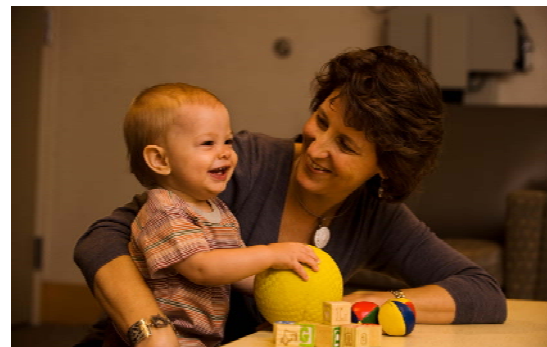
Naomi Ekas Ph.D., Postdoctoral Fellow

Sally Ozonoff, UC Davis

Mark Shen, Doctoral student
Christine Wu-Nordahl, Ph.D.
A.J. Schwichtenberg, Ph.D.

Joseph Piven, UNC

Jed Elison, Doctoral student, (UNC)
Jason Wolff, Doctoral student (UNC)



Sally Ozonoff and a toddler during a study to investigate early signs of autism

Shanna Alvarez, Doctoral student (UW)
Tanya St. John, Doctoral student (UW)

SunHyung Kim, Postdoctoral fellow (UNC)
Mahshid Farzinfar, Postdoctoral fellow (UNC)
Neda Sadhegi, Postdoctoral fellow (Utah)
Anuja Sharma, Postdoctoral fellow (Utah)
Julia Parish-Morris, Postdoctoral fellow (CHOP)

Marian Sigman, UCLA

Kristen Gillespie-Lynch – Doctoral student
Ted Hutman, Postdoctoral fellow

Wendy Stone, Vanderbilt University

Cara Damiano – Doctoral student
Elizabeth Malesa – Doctoral student

Elizabeth Catania PhD – Postdoctoral fellow
Lisa Ibanez PhD – Postdoctoral fellow

Mark Strauss, University of Pittsburgh

Desiree Wilkinson – Doctoral student
Sarah Hannigen – Doctoral student

Holly Gastgeb PhD. – Postdoctoral fellow

Helen Tager-Flusberg, Boston University

Anne Seery – Doctoral student (BU)
Meagan Thompson – Doctoral student (BU)
Beverly Wang – Doctoral student (BU)
Sharon Fox – MD/PhD student (Harvard/MIT)
Adrienne Tierney – Doctoral student (Harvard)

Rhiannon Luyster – Postdoctoral Fellow
Jennifer Wagner – Postdoctoral Fellow
Guilia Righi – Postdoctoral Fellow

Sara Jane Webb, University of Washington

Karen Burner, Doctoral student

Emily Jones, PhD, Postdoctoral fellow
Tanya St. John, PhD, Postdoctoral Fellow

Nurit Yirmya, Hebrew University

Maya Yaari - Doctoral student

Ifat Seidman – Postdoctoral fellow

Lonnie Zwaigenbaum, University of Alberta

Shelley Mitchell – Doctoral student (University of Toronto)

Stelios Georgiades – Doctoral student (McMaster University)

AS Toddler Treatment Network: Report Update

In 2010, the Toddler Treatment Network met by teleconference on a quarterly basis to discuss the development of the goals, objectives and directions of the network, and to share preliminary analyses of data collected so far from these randomized trials. There are two major commonalities across the studies: (1) they are parent-implemented, and (2) they all involve naturalistic delivery of interventions addressing the earliest autism behavioral phenotype and thus are heavily focused on communication: joint attention, imitation, gestures and language. The projects use different intervention models, most of which involve adaptations of existing preschool interventions to make them more infant-appropriate. The intervention involve techniques that can be implemented outside the clinic, allowing parents and caregivers to use these techniques in different settings, decreasing the time between parent's initial concern and beginning intervention, thus hopefully improving developmental outcome in the long run. Because they require less "in clinic" time, they may also be very cost effective. A summary of each of these projects can be found here:

http://www.autismspeaks.org/science/research/initiatives/toddler_treatment_network.php

The overarching goals of the network are to a) improve measurement tools regarding outcomes for toddlers and their families, b) define or identify best practices for designing and implanting efficacious parent-delivered interventions, c) improve research designs and analytic approaches for early intervention studies, d) facilitate young researchers to develop productive programs of high quality treatment research and e) disseminate evidence of efficacy of early intervention with toddlers. As there are similarities in outcome measures, methods of intervention and study design, in addition to discovering project-specific effects, the group prepared to combine data across sites. This included calculation of effect sizes (difference between performance before intervention and after) from all sites and a tutorial on mediation analysis from a statistical expert at the University of Arizona.

Autism Speaks awarded a grant to Sally Rogers at UC Davis to lead a combined meta-analysis effort across TTN sites. This structure of the TTN is an ideal situation for meta-analysis, which seeks to estimate the population treatment effect size and identify and estimate the covariates of treatment effect sizes. A meta-analysis across these studies will provide answers to the broader question of the efficacy of parent-mediated interventions compared to community interventions. This will very important to this group of studies, many of which have too few subjects to fully power analyses from individual projects. Effect sizes of the intervention and global functioning of the children in the study

will be combined with covariates including autism severity and estimates of treatment intensity to determine if differences in these covariates across sites contributed to differences in the outcomes.

Collaborative Projects (2010)

A: **Prospective Study of Head Circumference in Infants at Risk for ASD**

Project Leader: Lonnie Zwaigenbaum

Working group: Lonnie Zwaigenbaum, Wendy Stone, Karen Dobkins, Sally Ozonoff (new member),

This was the first collaborative data project of the BSRC. Supplemental funds were provided by AS to set up the data management team and database at Vanderbilt University. Current analyses indicate atypical increased head circumference in infant siblings of children with ASD compared to low-risk infants with no family history of ASD. However, it does not appear that increased HC is associated with the likelihood of autism among infant siblings in this particular sample. An abstract was presented at IMFAR 2008. An additional funding supplement was awarded by AS to update the data to reflect current outcome status in participating high-risk and low-risk infants, finalize quality control, and conduct additional analyses. With funding in 2010 to create a BSRC database, these tasks were transferred to UC Davis (Gregory S. Young, PI) and analyses are being finalized. It is expected that a draft of a manuscript from this project will be completed and submitted for publication in 2011.

B: **BSRC DNA Biorepository**

Project Leader: Lonnie Zwaigenbaum

Working Group: Lonnie Zwaigenbaum, Sally Ozonoff, Rebecca Landa, Daniel Messinger, Wendy Stone, Karen Dobkins, John Constantino, Zachary Warren

There has been substantial progress in identifying ASD susceptibility genes; specifically, rare de novo and inherited 'copy number variants' (CNVs) involving neuronal synaptic genes. These rare variants appear to be highly penetrant, and collectively, account for a significant proportion of ASD cases. If genetic biomarkers could be used to identify infants likely to develop ASD, this could revolutionize opportunities for earlier diagnosis and treatment. Thus, advances in genetic research, coupled with the availability of high-risk infant cohorts, have created the unique opportunity to test the predictive validity of genetic variants for ASD diagnoses.

Preliminary discussion regarding the potential benefits of a genetics repository developed as part of the 'Gene Environment Contributions to Risk for Autism (GECRA) initiative, supported by Autism Speaks. In 2009, a grant was submitted to NIH to support the collection and analysis of DNA samples from a subset of the BSRC participating sites. The grant received favourable reviews however it was not funded. Following further planning, 6 BSRC sites, working together with leadership from the Autism Genome Project (AGP; Drs. Stephen Scherer and Joachim Hallmayer) developed a proposal to establish a biorepository including DNA, cell lines and plasma samples, to conduct

genomic analyses aimed at detecting high-risk CNVs in these families, and then to assess the clinical utility of these variants for early diagnosis. A 3-year grant has been submitted to the Simons Foundation Autism Research Initiative (SFARI), and a letter of intent has been submitted to Autism Speaks (Basic and Clinical Science Operating Grants).

C. Developmental Outcomes in Later-born Siblings of Children with ASD

Project Leaders: Sally Ozonoff and Nurit Yirmiya

At the December 2007 Meeting, several BSRC sites presented data on developmental outcomes of siblings at risk. It was agreed that this topic would be the focus of a collaborative project, as a primary project for the Consortium. During 2008, data were collected from all sites that had outcome data on at least a portion of their sample. In 2009, a database was created to merge data across sites, data were cleaned, and analyses performed. Final results were obtained in 2010 and submitted for publication. Data from 664 infants with an older sibling with autism were included in the final analyses. 18.7% of infants developed an ASD. Infant sex and the presence of more than one older affected sibling were significant predictors of ASD outcome, with an almost three-fold increase in risk for males and an additional two-fold increase in risk if there was more than one older affected sibling. In contrast, the age of the infant at study enrollment, the sex and functioning level of the infant's older sibling, and other demographic factors did not predict ASD outcome. This data, pooled across 12 sites, indicates that the sibling recurrence rate of ASD is higher than suggested by previous estimates. The paper is currently under review at *Pediatrics*.

Goals for 2011

Based on discussions at the annual meeting held this year in January 2010 the following goals were set for the BSRC:

1. Explore funding options for the collection of genetic samples from BSRC participants.
2. Develop and implement a set of common measures that all BSRC sites collect.
3. All sites make initial data contributions to database
4. Develop multiple secondary projects, including pooled analysis examining stability of early diagnosis