Executive Summary

1. The BSRC incorporated in November 2005 now includes 23 members on the Committee of Principal Investigators.
2. To date, approximately 2385 siblings at risk for ASD have been enrolled in our research programs. We expect approximately 560 additional siblings will be enrolled in the coming year.
3. In 2008, members of the BSRC published 39 papers or book chapters on topics directly relevant to the mission of the Consortium. A special issue of the journal, *Autism: The International Journal of Research and Practice* was published on Early Detection of Autism, edited by two members of the BSRC CPI (Zwaigenbaum and Stone). In addition, members of the BSRC gave 68 presentations at conferences.
4. 18 new grants were awarded to members of the BSRC in 2008, relating to projects relevant to the BSRC.
5. In 2008, 34 graduate students and nine post-doctoral or clinical fellows were engaged in research programs associated with the BSRC. Through their participation, members of the BSRC CPI have committed to training the next generation of researchers in this critical area.
6. The AS Toddler Treatment Network made significant progress during the year.
7. The GECRA Project (Genetic and Environmental Contributions to the Risk for ASD) was completed culminating in a final report that summarized four novel projects that were highlighted as high priority feasible opportunities for the BSRC to lead.
8. There are three ongoing collaborative projects in the BSRC covering the following topics:
   a. Prospective study of head circumference in infants at risk
   b. Prospective study of genetic and environmental factors in infants at risk
   c. Developmental outcomes in siblings of children with ASD

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 behavioural 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 identify new
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
Kasia Chawarska, Ph.D.                                   Yale University
John Constantino, M.D.                                  Washington University
Karen Dobkins, Ph.D.                                     UCSD
Deborah Fein, Ph.D.                                      University of Connecticut
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.                                       Vanderbilt University
Mark Strauss, Ph.D.                                      University of Pittsburgh
Helen Tager-Flusberg, Ph.D.                              Boston University
Sara Webb, Ph.D.                                          University of Washington
Nurit Yirmiya, Ph.D.                                     Hebrew University, Jerusalem Israel
Lonnie Zwaigenbaum, M.D.                                 University of Alberta, Edmonton, Canada

One new member was admitted to the BSRC this year: Suzanne Curtin, Ph.D., University of Calgary

Autism Speaks Project Staff
Geraldine Dawson, Ph.D.
Alicya Halladay, Ph.D.
Andy Shih, Ph.D.

NIH Project Staff
NICHD: Alice Kau, Ph.D.
External Advisory Committee
The three year terms of the previous advisory committee had ended in 2008, so new members were elected to our advisory board:

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 2008-9) include:

Chair Lonnie Zwaigenbaum
Co-Chair Helen Tager-Flusberg
Project Liaison Sally Ozonoff

Participants in BSRC Projects
We have enrolled 2385 siblings at risk for ASD, the majority of whom are still actively being following. In addition, almost 500 infants from “low risk” or non-affected families are included in BSRC studies.

In the coming year, we expect to enroll an additional 560 siblings.

Annual Meeting Summary
The BSRC held its annual meeting in San Francisco, Calif. on December 6 and 7 of 2007. This meeting focused on the challenges behind examining developmental trajectories in infants, and eventually led to the creation of a draft primary project for the consortium. In addition, Craig Newschaffer engaged the entire BSRC regarding the newly funded ACE award examining a host of environmental factors during prenatal development in siblings at risk for developing autism.
Paper Published in the Journal Pediatrics

Under the leadership of Lonnie Zwaigenbaum, members of the BSRC worked collaboratively on a highly significant paper to be published in the May, 2009 issue of the journal Pediatrics. This paper titled: “Clinical assessment and management of toddlers with suspected autism spectrum disorder: Insights from studies of high-risk infants” is the first paper to disseminate findings from the BSRC to the wider clinical community.

Publications in 2008

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

In 2008, the journal Autism (official publication of the National Autistic Society) published by Sage devoted a special issue to the topic of “Early detection of Autism”, Lonnie Zwaigenbaum and Wendy Stone (members, CPI) were the editors of this special issue. The entire issue is offered free of charge by visiting the Autism website http://aut.sagepub.com/content/vol12/issue5/

(**These publications are authored by more than one member of the BSRC CPI.)

Susan Bryson


Alice Carter


Kasia Chawarska and Ami Klin (Yale Child Study Center)


Deborah Fein


Rebecca Landa


Daniel Messinger
Sally Ozonoff


Joseph Piven


Sally Rogers


**Wendy Stone**


**Helen Tager-Flusberg**


**Sara Webb**

Lonnie Zwaigenbaum


Conference Presentations in 2008

Susan Bryson


**Drummond, K., Roberts, W., Brian, J., Bryson, S., Roncadin, C., Smith, I.M., Szatmari, P. and Zwaigenbaum, L. Varying Pathways to Asperger’s Syndrome at Age 5: A Prospective...


Alice Carter


Kasia Chawarska and Ami Klin (Yale Child Study Center)


Karen Dobkins and Leslie Carver (UCSD)


Deborah Fein


February) *Differentiating ASD from other developmental delays in young children.* Poster presented at the meeting of the International Neuropsychological Society, Waikoloa, HI.


**Jana Iverson**


Rebecca Landa


Daniel Messinger


Sally Rogers


**Marian Sigman/Ted Hutman (UCLA)**


Wendy Stone


Mark Strauss


Helen Tager-Flusberg


Nurit Yirmiya


Lonnie Zwaigenbaum


Newly Funded Grants in 2008

The following grants were awarded to members of the CPI during 2008 to support their research on infants at risk for ASD.

**Susan Bryson**  
**Bryson, S.E. (Co-investigator with PI C. Roncadin)**  
Ontario Mental Health Foundation.  
Title: Discriminating Autism from Other Atypical Patterns of Development in a Community Sample  
$142,005 (2008-10)

**Karen Dobkins**  
NIH/NICHD R01 HD052804-01A2  
Title: Development of Neural Pathways in Infants at Risk for Autism Spectrum Disorders  
Total Funding Amount: $1,313,252 (1/1/08 – 1/1/12)

**Ami Klin and Kasia Chawarska**  
National Institute of Mental Health RO1 MH 083727  
Title: The Ontogeny of Social Visual Engagement in Infants at Risk for Autism  
$3,547,500 (07/01/2008 - 06/30/2013)

**Daniel Messinger (Wendy Stone Co-PI)**  
NICHD RO1HD057284  
Title: Social-Emotional Development of Infants At Risk for Autism Spectrum  
$1,250,000 to U. Miami (2008-2013).

**Joseph Piven**  
NIH Supplement to ACE Network  
RO1 HD055741-S1  
Title: A Longitudinal MRI Study of Infants at Risk for Autism  
$512,358 (7/1/08-6/30/13)

Autism Speaks Supplement  
Title: CROSS: The IBIS-EARLI Collaboration  
$449,886 (1/1/09-12/31/11)

Simons Foundation Supplement  
Title: A Longitudinal MRI Study of Infants at Risk for Autism  
$150,000 (7/1/08-6/30/13)
Wendy Stone  
** NICHD R01 HD057284 (Stone & Messinger – Co-PIs)  
Title: Social-Emotional Development of Infants At-Risk for ASD  
$2,424,332 (2008-2013)  

Mark Strauss  
NICHD (P50)  
Title: Biological and Information Processing Mechanisms Underlying Autism.  
$1.5 million (8/2007-7/2012)  

Autism Speaks  
Title: Mentor Grant: Development of categorization and facial knowledge in infants at-risk for autism  

Helen Tager-Flusberg  
Autism Speaks  
Title: Novel Measures for Testing Language Comprehension in Children with Autism Spectrum  
$450,000 (7/1/08-6/30/11)  

Sara Webb  
Washington State Legislative Initiative: Developmental Disabilities Project  
Title: Electrophysiological risk markers in infant at risk for autism  
6/09-9/09  

Washington State Legislative Initiative: Developmental Disabilities Project  
Title: Does atypical head growth predict autism symptoms and severity?  
6/09-9/09  

NIH 5-P30 ES007033-14, Eaton (PI)  
Title: Infant exposure to plasticizers as potential contributors to autism spectrum disorders  
4/08-3/09  

Autism Speaks Mentors’ Program, Postdoctoral Fellowship, Webb/Murias (PI)  
Title: The use of ERPs to investigate outcome in children with autism  
3/08-2/10
Nurit Yirmiya  
United States-Israel Binational Science Foundation.  
Title: Characteristics of the broad autism phenotype (BAP) in siblings of children with autism.  
$142,000 (2008-2010)

Lonnie Zwaigenbaum  
Ontario Mental Health Foundation. (Co-investigator with PI C. Roncadin)  
Title: Discriminating Autism from Other Atypical Patterns of Development in a Community Sample  
$142,005 (2008-10)

Canadian Institutes of Health Research. (co-PI with D Nicholas).  
Title: A Synthesis Review of Interventional Outcomes in Childhood Autism.  
$100,000 (2008-09)

**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.

**PI: Susan Bryson, Dalhousie University**  
Graduate Students  
Shelley Mitchell, MSLP (speech language pathology – at Toronto site)

Post-doctoral Fellow  
Nancy Garon, Ph.D (developmental psychology)  
Ghassan Kuwaik, M.D. (developmental pediatrics – at Toronto site)

**PI: Leslie Carver, UCSD**  
Graduate Student  
Lauren Cornew

**PI: Suzanne Curtin, University of Calgary**  
Graduate Student  
Danielle Droucker (Applied Psychology)

**PI: Deborah Fein, University of Connecticut**  
Graduate Students
Katelin Carr  
Kelley Knoch

**PI: Jana Iverson, University of Pittsburgh**  
Graduate Students  
Nina Leezenbaum (Psychology)  
Erin Koterba (Psychology)  
Meaghan Parladé (Psychology)  
Jana Rea (Psychology)

**PI: Rebecca Landa, Kennedy Krieger Institute/Johns Hopkins University**  
Postdoctoral Fellow  
Anjana Bhat, M.D.

**PI: Catherine Lord, University of Michigan**  
Graduate Students  
Kristina Lopez (Psychology)  
Themba Carr (Psychology)  
Meghan McDonald (Kinesiology)  
Melissa Carrusco (MD/PhD)  
Sarah Luchansky (Social Work)

**PI: Daniel Messinger. University of Miami**  
Graduate Students  
Lisa Ibanez, (Psychology)  
J.D. Haltigan, (Psychology)  
Caroline Grantz, (Psychology)  
Nicole McDonald, (Psychology)  
Steven Cadavid, (Psychology)

Postdoctoral Fellows  
Mohammad Mahoor, M.D.  
Jason Baker, M.D.

**PI: Sally Ozonoff, UC Davis/MIND Institute**  
Postdoctoral Fellows  
AJ Schwichtenberg, Ph.D  
Giacomo Vivanti, Ph.D

**PI: Joseph Piven, University of North Carolina**  
Graduate Student  
Jed Elison (Psychology)

Postdoctoral Fellow  
Deb Childress, Ph.D.
PI: Marian Sigman, UCLA
Graduate Students
Lisa Christensen (Psychology)
Mari Davies (Psychology)
Kristen Gillespie-Lynch (Psychology)
Leigh Sepeta (Psychology)

Postdoctoral Fellow
Ted Hutman, Ph.D.

PI: Wendy Stone, Vanderbilt University
Graduate Students
Allison Presmanes (Psychology)
Lauren Turner Brown (Psychology)
Caitlin McMahon (Psychology)
Jennifer Foss-Feig (Psychology)
Elizabeth Malesa (Psychology)
Cara Damiano (Psychology)
Allison Nahmias (Psychology)

Postdoctoral Fellows
Lynnette Henderson, Ph.D.
Elizbeth Catania, Ph.D.

PI: Mark Strauss, University of Pittsburgh
Graduate Students
Catherine Best (Psychology)
Holly Gastgeb (Psychology)
Keiran Rump (Psychology)
Desiree Wilkinson (Psychology)
Sarah Hannigen (Psychology)

PI: Helen Tager-Flusberg, Boston University
Graduate Students
Meaghan Thompson (Psychology)
Anne Seery (Psychology)

PI: Nurit Yirmiya, The Hebrew University of Jerusalem
Graduate Students
Ifat Gamliel (School of Education)
Raaya Alon (School of Education)

PI: Lonnie Zwaigenbaum, University of Alberta
Graduate Students
Shelley Mitchell, MSLP (speech language pathology – at Toronto site)

Post-doctoral Fellow
Ghassan Kuwaik, M.D. (developmental pediatrics – at Toronto site)
AS Toddler Treatment Network: Report Update

In February of 2008, the Toddler Treatment Network, which includes some but not all members of the BSRC, met in San Diego, Calif. to discuss the goals, objectives and directions of the network. 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. Investigators in the TTN are working on improving or expanding on diagnostic and outcome measures so that comparisons across the studies can be made. 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 under “science initiatives” at www.autismspeaks.org. In 2008, the network established a set of common overarching goals, which includes, but was not limited to:

1. Improving measurement regarding outcomes for toddlers with autism and their families on both comprehensive outcome measures and core deficits of autism. This includes adding and refining measurements, identifying common and unique measures, and facilitating training across sites. This was accomplished through a group training on the ADOS for toddlers (facilitated by Cathy Lord) as well as the completion of a non-common measures table. This non-common measures table shares with others new or unique measurements that allow each group to provide a unique insight into aspects of successful intervention.

2. Defining best practices for designing and delivering parent-implemented interventions with autism. The groups have shared a number of common measurements or novel intervention techniques, posted privately and accessed by all TTN members.

3. Improving research designs and analytical approaches for early intervention studies. With the help of Paul Yoder, groups participated in a questionnaire to share randomization procedures which was shared across sites, and Hannah Schertz polled the group and provided information on how sites are conducting fidelity measurements.

4. Facilitating young researchers in the field. Michael Siller from Hunter College wrote and finalized a publication agreement that will be used
from the site to share information that can be shared with a larger audience.

This group meets via teleconference bi-monthly to discuss challenges, ideas, and potential opportunities for sharing of information. In addition, in 2008 Autism Speaks announced an RFA in treatment research that will enhance, improve, or expand these existing studies, or perhaps build on existing collaborations within the group. While the findings of the group are still preliminary, they are promising and provide a possible cost-effective, efficient and effective way of providing much needed services to toddlers from the ages of 18-24 months.

**Collaborative Projects (2008)**

**A: Prospective Study of Head Circumference in Infants at Risk for ASD**  
Project Leader: Lonnie Zwaigenbaum  
Steering committee: Lonnie Zwaigenbaum, Wendy Stone, Karen Dobkins, Rick Urbano, Warren Lambert

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. The initial set of analyses have been completed, demonstrating atypical patterns of growth in head circumference toward the end of the first year of life, especially in those infants who later meet criteria for a diagnosis of autism. An abstract was presented at IMFAR 2008. An additional funding supplement has been 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. It is expected that a draft of a manuscript from this project will be completed and submitted for publication in 2009.

**B: Gene Environment Contributions to Risk for Autism (GECRA)**  
Project Leader: Lonnie Zwaigenbaum  
Steering Committee: Lonnie Zwaigenbaum, Helen Tager-Flusberg, Ezra Susser (Columbia U), Alycia Halladay (AS), Andy Shih (AS), Geraldine Dawson (AS)

With support of the planning/feasibility grant from Autism Speaks, a two-day meeting was convened between the steering committee, external advisors, and BSRC investigators and invited collaborators from their home institutions identified as potential contributors to the GECRA research agenda. Observers from Autism Speaks (including scientific leadership) also participated.
The first day of the meeting was devoted to scientific presentations and small group discussions. Presentations covered a wide range of topics relevant to environmental risk research, delivered by External Advisors to GECRA who include leading experts in their respective fields:

Dr. Glenn Rall – immunology  
Dr. Salvatore DiMauro - mitochondrial disorders  
Dr. Carolyn Schanen – epigenetics  
Dr. Roberta White – environmental toxicology  
Dr. Peter Szatmari – genetics  
Dr. Lisa Croen – risk factors in high-risk cohorts – retrospective design  
Dr. Craig Newschaffer – risk factors in high-risk cohorts – prospective design

Following these presentations, conference participants broke into small groups for more focused discussion focusing on methodology, feasibility and potential research questions. The groups were divided into: genetics, immunology, and environmental risks. The Steering Committee collated the summaries of the small group discussions, and synthesized the scientific ideas that were generated into a set of projects.

The second day of the meeting began with a detailed presentation of the BSRC studies and cohorts, followed by a summary presentation of eight potential project ideas that emerged from the previous day’s presentations and discussion groups. Based on the uniqueness of the infant sib/high risk cohort for answering these questions, state of the current science, expertise of members and/or collaborators, as well as enthusiasm of the CPIs in participating, four projects were chosen for further examination:

Projects:
1. Collection and banking of DNA samples
2. Screening for mitochondrial mutations and diseases
3. Investigation of vaccination rates and association with diagnostic outcomes
4. Pre- and peri-natal risk factors associated with ASD

The remainder of the meeting was devoted to more detailed group discussion of these ideas, refining the hypotheses and methodologies that could be fruitfully explored, in the context of the BSRC cohorts. A feasibility report was generated at the end of 2008 which included possible sample sizes, logistical issues, and budget scenarios based on interested participating sites.

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. This project is now in progress – data are currently being cleaned and checked and preliminary statistical analyses are underway.

**Goals for 2009**

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. This project is now in progress – data are currently being cleaned and checked and preliminary statistical analyses are underway.

(i) Complete the Head Circumference and Developmental Outcomes collaborative projects. Dissemination of the findings from these projects.

(ii) Progress on the Treatment network

(iii) Application for funding to support component projects of GECRA

(iv) Establish a long-term database that will support all current and future projects of the BSRC.

**Acknowledgments**

The research conducted by members of the BSRC is largely supported by funds from Autism Speaks and the National Institutes of Health. We gratefully acknowledge the support of these and several other agencies and foundations for our individual research programs. We thank members of our External Advisory Board for their advice on our current programs. The activities of the BSRC are made possible by the generous support of Autism Speaks. We are especially grateful to Alycia Halladay and Andy Shih for their encouragement and tireless activity on our behalf.