Research on Tap: Current Research on Autism at Boston University: From Cells to Society

November 1, 2018

Boston University Office of the Vice President and Associate Provost for Research

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From Cells to Society

Helen Tager-Flusberg

Professor
Psychological & Brain Sciences, CAS

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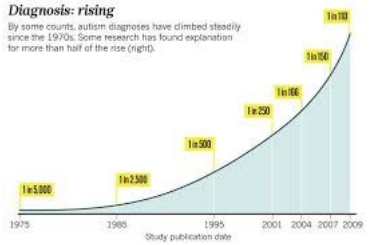
How we got here...

Bauman & Kemper (1998/2002) *Neuropathology of infantile autism*

- Leaders in the field – pioneers in post-mortem analyses of the brain
- Highlighted role of cerebellum, limbic system; changes in brain size
- Work continued with Gene Blatt, students, and other collaborators



2001 – Clinical research programs on ASD

- Department of Anatomy & Neurobiology
- Rates are rising; NIH is now funding research

2009 - Moved lab to CRC – now CARE

- Expanded network of clinicians, researchers, scholars all with shared interests in autism

Goals for today...

Showcase - the wide-ranging interests and work on autism at BU

Network – discuss common goals; further collaborations

Future – how can we further advance what each of us is doing and how can we develop new directions

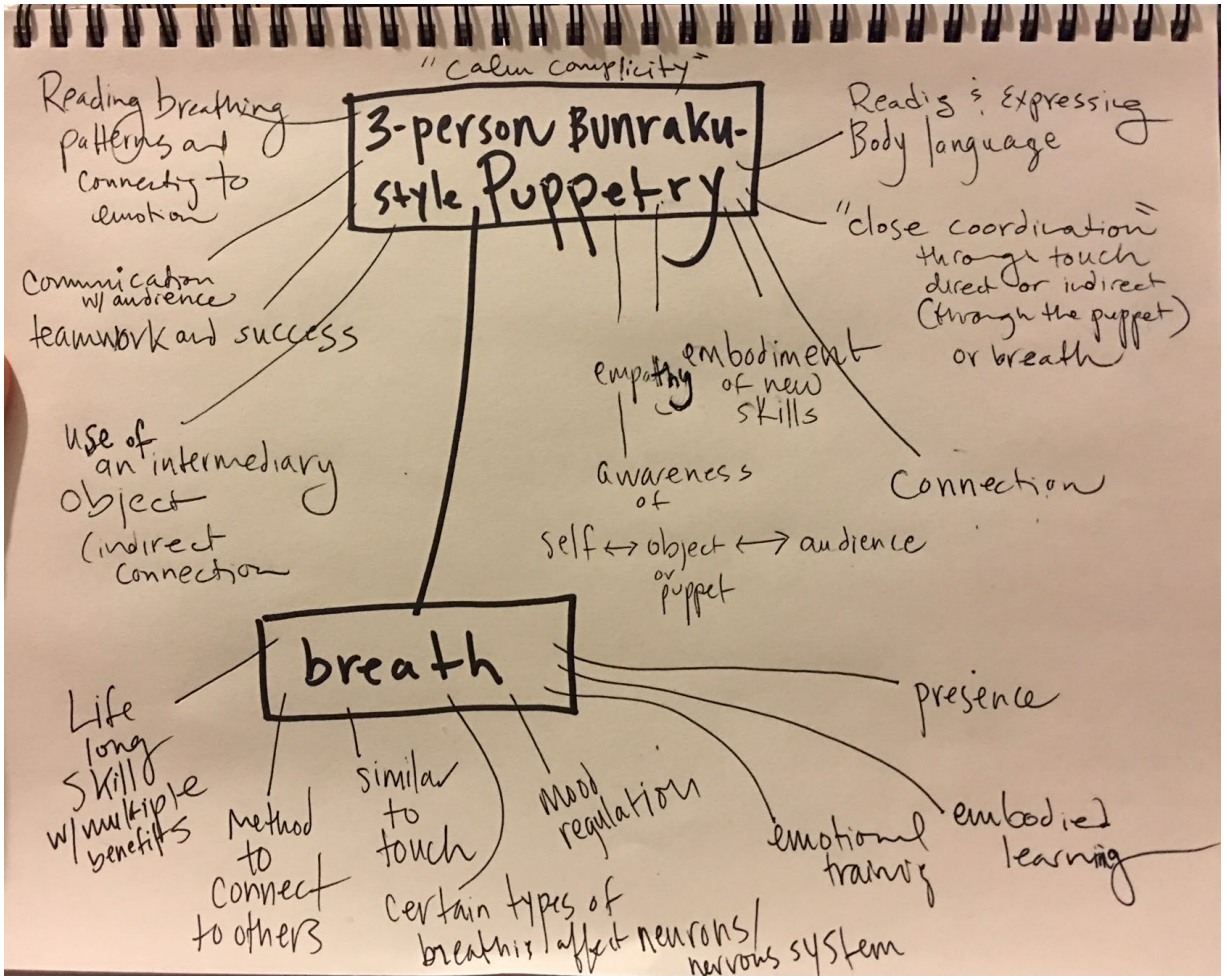
Puppets for Building Awareness of Self and Others

Dr. Felice Amato

Assistant Professor
Art Education, SVA/CFA

A Puppeteer Asks Research Questions

Students with a puppet and the professional company Blind Summit



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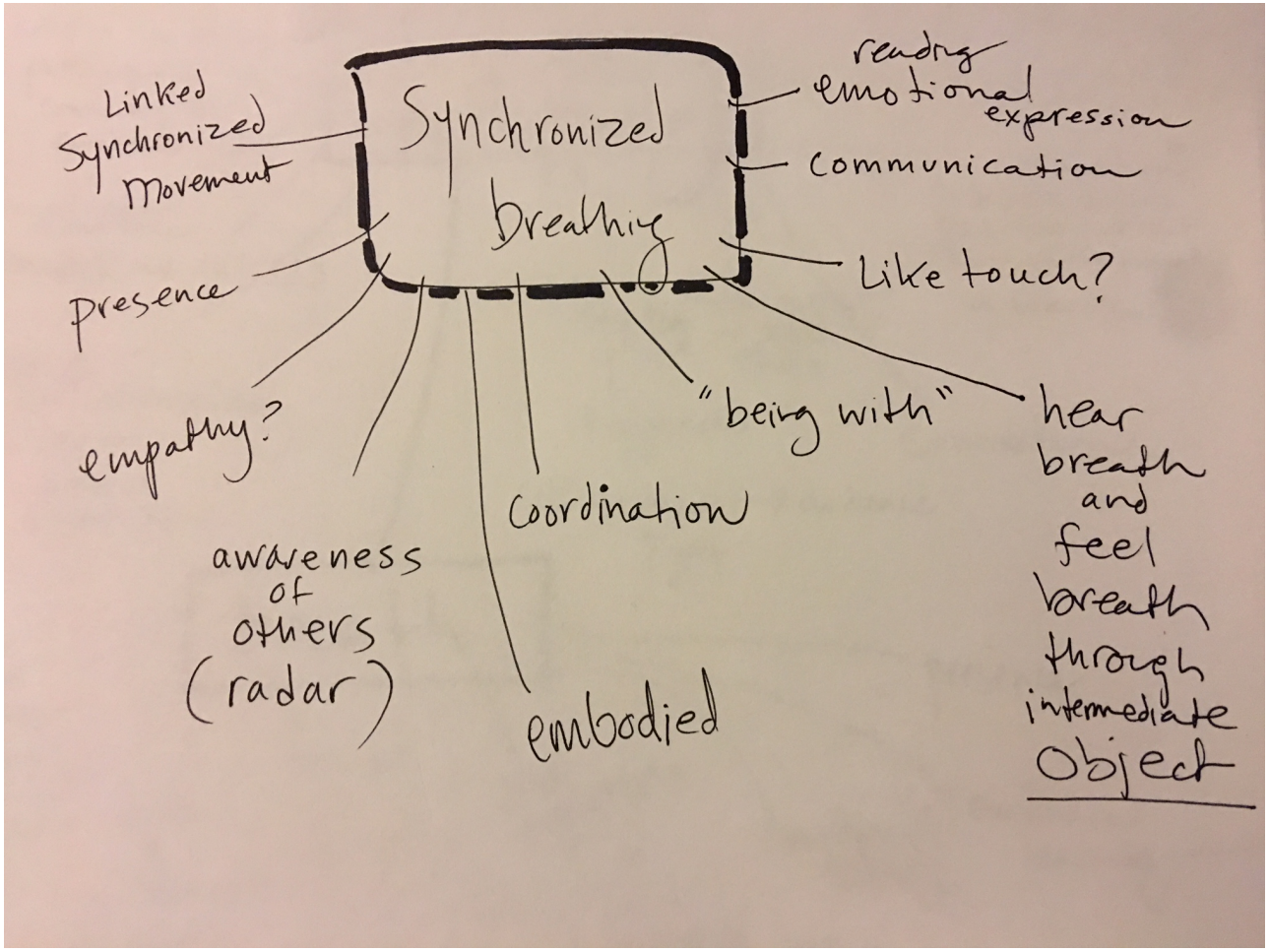
In 3-person, Bunraku-style puppetry, everyone's hands are on the puppet and everyone breathes together.



Could participation in 3-person Bunraku-style puppetry allow a student with autism to develop skills in synchronized breathing?

Could this and other puppetry skills contribute to

- mood regulation?
- attunement to others?
- Empathy?
- Reading/sensing emotion and its connection to breath and movement?

Could the intermediary of the puppet and breath lead to connection that has similar qualities to touch (but isn't touch)?

Is embodied acquisition of these skills as valuable or more valuable than other ways of acquiring them ?

Creating an Autism Friendly Hospital: What it takes and how to get there

Marilyn Augustyn

Professor Of Pediatrics
Boston University School of Medicine

Division Director, Developmental and Behavioral Pediatrics
Boston Medical Center

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What it Takes: Understanding the Patient Journey

- Stakeholder Involvement
  - Parent Leadership in Autism Network
  - Hospital-wide Steering Committee
  - Quality Improvement Board
- Ethnographic Study
  - real-time challenges faced by patients with autism
  - utilizing observational methods and qualitative coding
- Patient Data Analysis
  - Using ICD-9 and ICD-10 codes, identified when, where, and how often patients with autism are being seen at Boston Medical Center
- Innovations in Care

How to Get There: Intervention Development, Testing, and Implementation

Based on the challenges identified through our needs assessment, we are pursuing a multi-pronged intervention based on the social-ecological model

Social Ecological Model	Pieces of the Intervention	Measurement/Approach
Individual	**Autism Support Checklist:** collects information about the patient's communication, sensory and safety needs and makes data available through electronic medical record	Studying implementation and effectiveness through Center for Implementation and Improvement (CIIS) grant
	Healthcare Social Stories App: Provides a preview of the hospital experience using social stories and populated with photographs of Boston Medical Center	User-tested by families associated with the Autism Program
Interpersonal	**Sensory Toolbox:** contains items including sunglasses, a weighted lap pad, for use by clinicians and staff with patients to make for a less stressful experience	Quality Improvement Methodology- conducting PDSA cycles
Organizational	**Trainings:** Intended to improve knowledge around autism and the needs of our patients, we offer a range of tailored trainings, many of which feature parent panels	Continuously soliciting feedback through questionnaires
Community/Policy and Practice Recommendations	**Learning Collaboratives:** Partner with other institutions to share knowledge **Publications and Conferences:** Publish and share efforts and results through journals and conferences	Collaborations with other institutions

Efforts to Improve Early Identification and Linkage to Services for Children with Autism Spectrum Disorder: the ASD PEDS Network

Sarabeth Broder-Fingert

Assistant Professor, Pediatrics, MED

Research on Early Identification and Linkage to Services for ASD: The ASD PEDS Network

Wendy Stone
Univ. of Washington

Karen Pierce
Univ of California San Diego
Southwest Autism Research & Resource Center

Alice Carter, Radley Sheldrick
Univ. of Mass. Boston
Tufts University

Sarabeth Broder-Fingert
Emily Feinberg
Boston University
Yale University
CHOP

Amy Wetherby, Ami Klin, Catherine Lord, Craig Newschaffer
Florida State University
Emory University
Drexel University
Weill Cornell Medical College

National Institute of Mental Health

Overview of Five ASD PEDS NETWORK Studies

PI	Study name	Intervention description	Screening tool(s) used	Age at screen	Target population	States	Region	Setting
Carter	Multi-stage screening for ASD in EI settings	Training EI providers to screen and refer for ASD diagnosis	Brief Infant-Toddler Social Emotional Assessment (BITSEA) (Giserman Kiss et al., 2017) and Parents' Observation of Social Interaction (POSI) (Sheldrick and Perrin, 2013)	14–33 months	EI providers	Massachusetts	Urban	Early intervention
Feinberg	Project early	Family navigation to improve access to diagnostic and treatment	Modified Checklist for Autism in Toddlers, Revised with Follow-Up (MCHAT-R/F) (Robins et al., 2014)	18 and 24 months	Primary/specialty providers and families	Massachusetts, Connecticut, Pennsylvania	Urban	Primary and specialty care
Pierce	Get set early model	Creation of a pediatrician learning network and referral center	Communication and Symbolic Behavior Scales Infant-Toddler Checklist (CSBS ITC)	12, 18, and 24 months	Primary care pediatricians	California, Arizona	Urban/sub-urban	Primary and specialty care
Stone	Screen-Refer-Treat (SRT) Model	Training primary care physicians in screening and early intervention providers in assessment and treatment	Modified Checklist for Autism in Toddlers, Revised with Follow-Up (MCHAT-R/F) (Robins et al., 2014) and Screening Tool for Autism in Toddlers (STAT) (Stone et al., 2004)	18–30 months	Primary care physicians and EI providers	Washington	Rural and urban	Primary care and early intervention
Wetherby	Mobilizing community systems to engage families in early ASD detection and services	Online provider training, screening, and provider/family navigator engagement tool	Early Screening for Autism and Communication Disorders (ESAC) (Wetherby et al., 2009)	12, 18, and 24 months	Primary care and community organizations and families	Florida, Georgia, New York, Pennsylvania	Urban and rural	Primary care, federally funded agencies, National Black Church Initiative (NBCI)

ASD: autism spectrum disorder; PEDS: Pediatric, Early Detection, Engagement, and Services; PI: principal investigator; EI: early intervention.

Broder-Fingert et al,
Autism, 2018

Autism in the US: Social Movement and Legal Change

Daniela Caruso

Professor of Law and EU Jean Monnet Chair
School of Law

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Legal Change: Examples

new frontiers

Individuals with Disabilities Education Act

Fed. Law + S.Ct. 2017:
"IEP → Progress!"

distributional problems

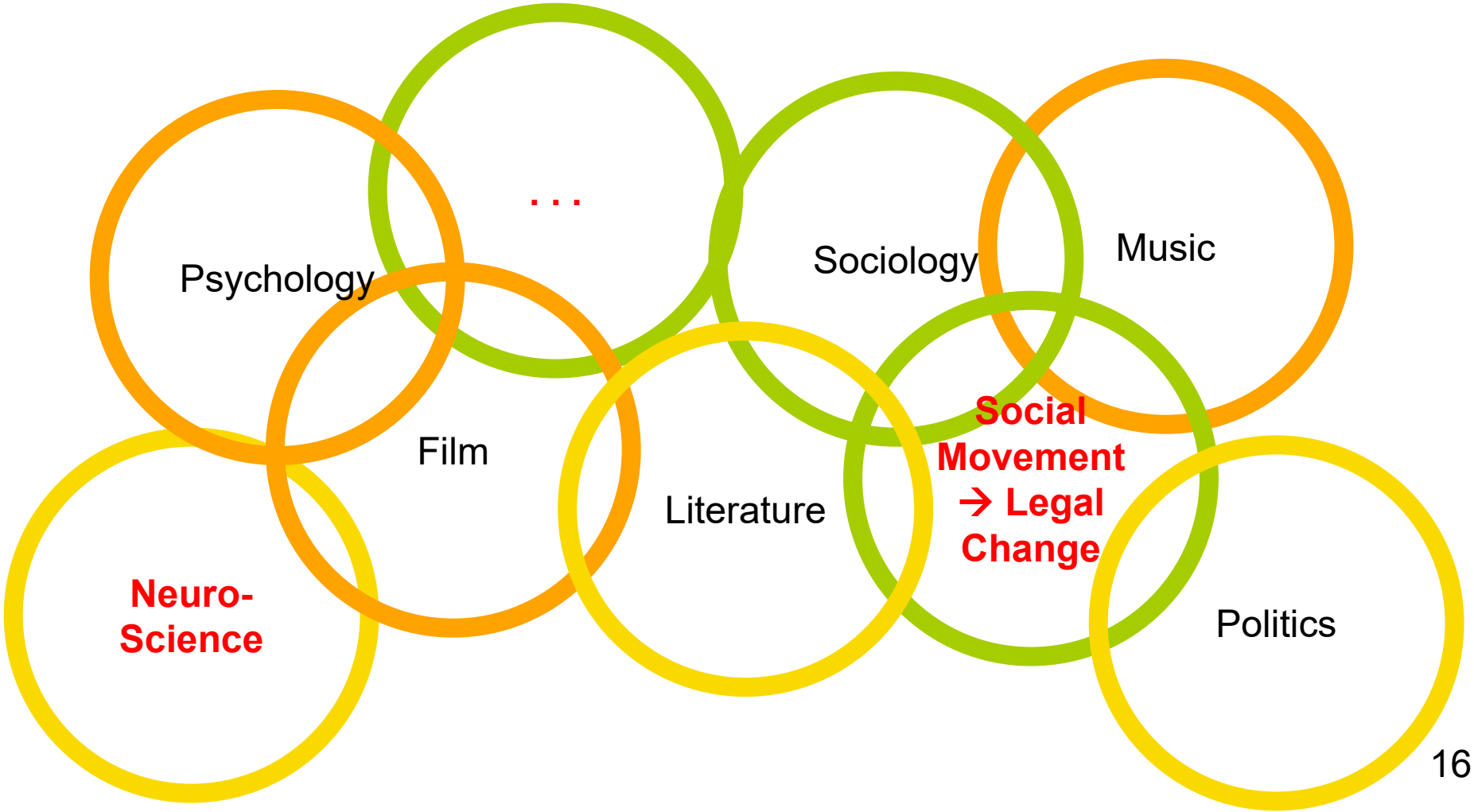
Medical Insurance Coverage of ABA

2010 ARICA

2015 MassHealth

MA Department of Developmental Services

IQ > 70 + substantial functional limitations =
Adult Services Eligibility since 2014


. . .
Psychology
Sociology
Music
Film
Literature
Social Movement → Legal Change
Neuro-Science
Politics

Autism in Adolescence and Adulthood: Social Contexts

Gael Orsmond

Associate Professor
Department of Occupational Therapy
College of Health and Rehabilitation Sciences: Sargent College

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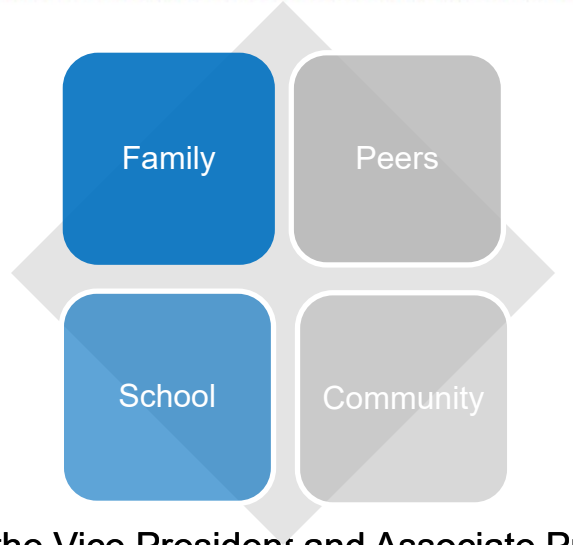
Families and Autism Research Lab

Research in the Families and Autism Research Lab (FAR) Lab focuses on contextual aspects of autism spectrum disorder (ASD) across the life course, such as family relationships, friendships, and social and community participation, especially during the transition from adolescence to adulthood.



- 4-year study funded by Institute on Education Sciences (*R324A160113*).
- Mixed-methods research to understand the education, supports, and outcomes of diploma-track high school students on the autism spectrum.
- Findings
  - Challenging to schools
  - Variability in approaches
- Recruiting longitudinal sample
- Will inform the development of programs and supports for this growing population

- MPI with Kristin Long
- 3-year study funded by NIMH (*R34MH111489)*
- To develop, assess feasibility, and examine outcomes of a program to engage adult siblings of persons with autism to work with families to plan for the future.
- Community-based; telehealth format
- Findings
  - Need for a program
  - Endorsement of approach
- Implementation of open trial

Autism: Enhancing Opportunities to be Engaged

Ellen S. Cohn

Clinical Professor
Department of Occupational Therapy
College of Health and Rehabilitation Sciences: Sargent College

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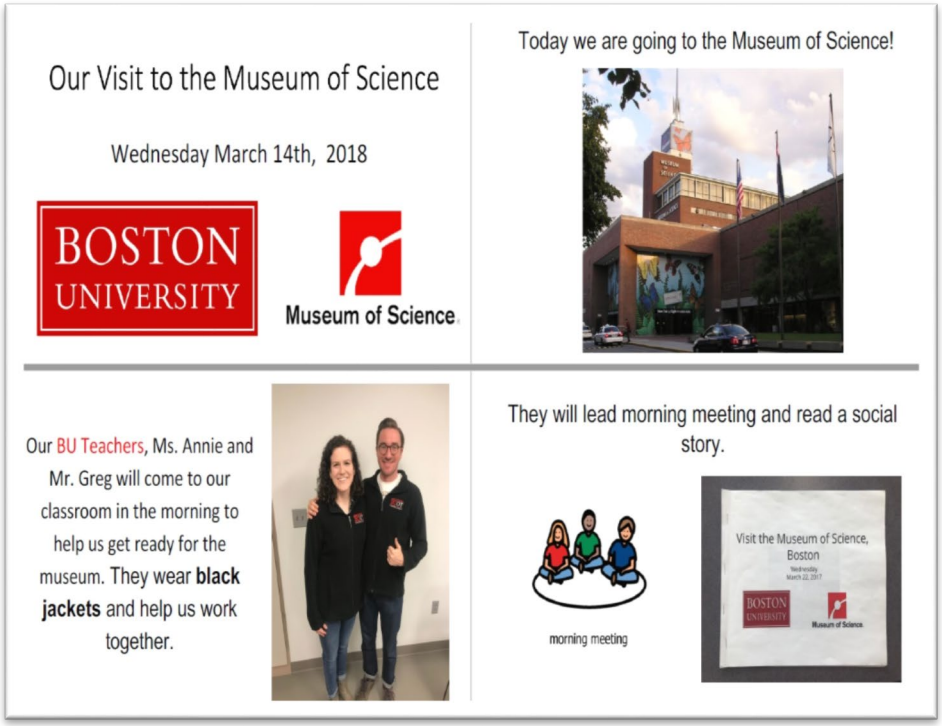
Videos of Important People (VIP) Intervention

- Combines **video self-modeling** and the **Video Intervention/ Prevention Assessment** (VIA; Rich et al., 2000)
- Self-generated videos and reflection
- Video self-modeling; excerpts from adolescents' self-generated videos to reinforce positive social behaviors
- Adolescents watch positive examples of themselves to engage in *positive self-review and self-reflection*

VIP Conceptual Framework

Buddies Exploring Science Together: BEST Program



Three BPS students work together at the MOS to complete a circuit—an example of the natural relationship between social and science learning.

Culture and Health Disparities in Autism Across the Lifespan

Kristin Long, PhD

Assistant Professor
Department of Psychological & Brain Sciences
College of Arts & Sciences

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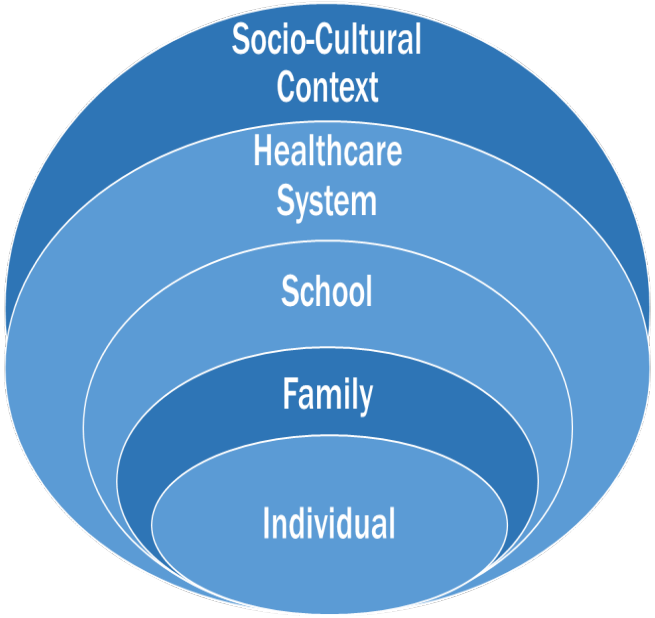
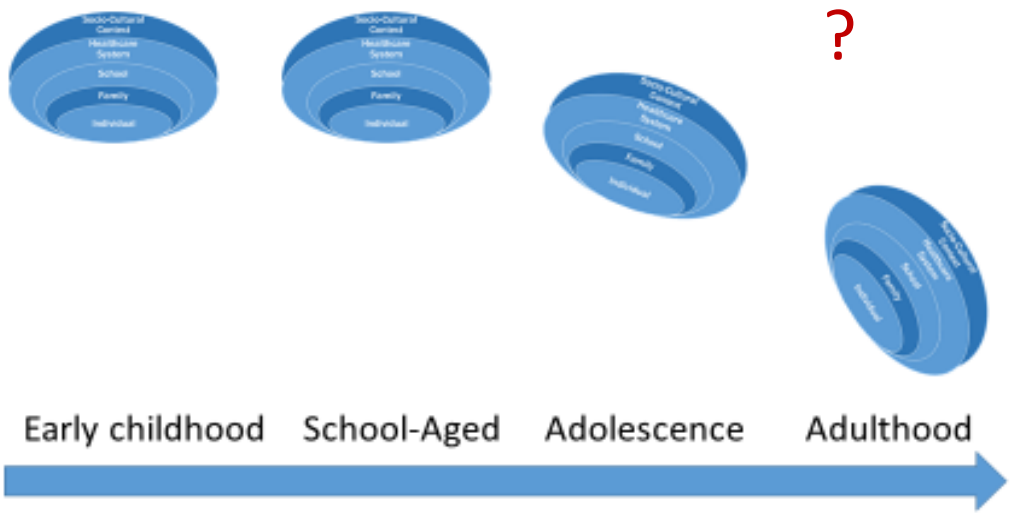
Social Ecology Model of Autism across the Lifespan

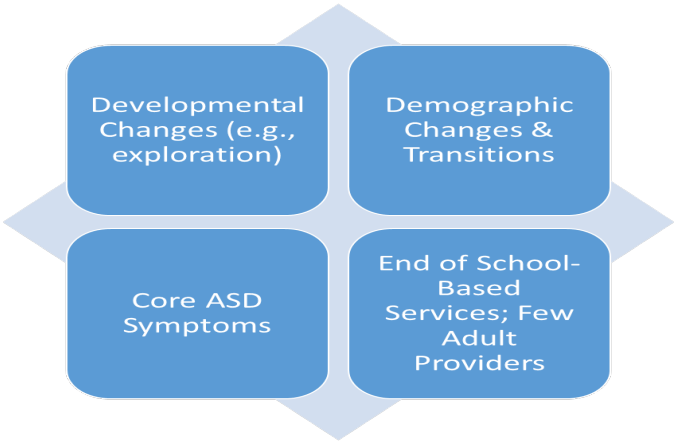


Entering adulthood = "Falling off the cliff"



Define disparity → Identify mechanisms → Apply to interventions

Racial, ethnic, & socioeconomic disparities over the transition to adulthood among youth with autism: A systematic review



- **Low-income** & **racial/ethnic minority** youth with autism less likely to:
  - Participate in transition planning meetings
  - Enroll in post-secondary education
  - Find competitive employment after HS
  - Live independently
  - Participate in social activities
  - Receive health care transition services

Eilenberg et al. (Under Review)

SIBLINGS FORWARD
FOCUSING ON RELATIONSHIPS, WELLBEING, AND RESPONSIBILITIES AHEAD

Latino families:

- Stronger future planning needs
- Latino siblings are well suited to engage in future planning
- Recs for *Siblings FORWARD*:
  - Increase parental involvement
  - Address services for undocumented immigrants
  - Emphasize autism education
  - Use active recruitment methods

Collaboration with Dr. Gael Orsmond (R34MH111489-S1)

Define disparity → Identify mechanisms → Apply to interventions

Autism Adaptive Community-based Treatment to Improve Outcomes using Navigators (ACTION) Network

Sarabeth Broder-Fingert
Emily Feinberg

Associate Professor, Community Health Sciences, SPH

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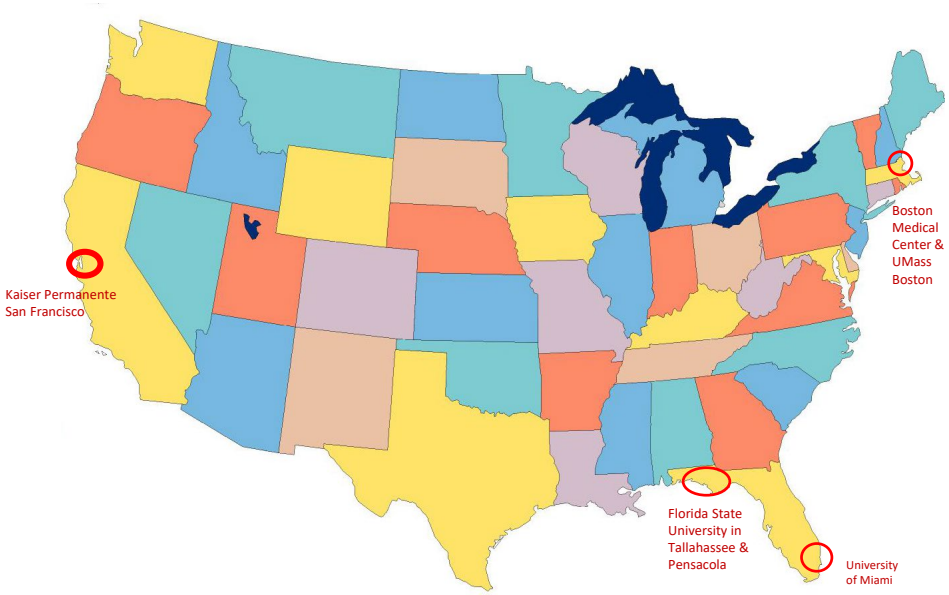
Autism *A*daptive *C*ommunity-based *T*reatment to *I*mprove *O*utcomes using *N*avigators (ACTION) Network



NIH Autism Center of Excellence (ACE) grant that supports large-scale multidisciplinary studies on autism spectrum disorders (ASDs), with the goal of determining the disorders' causes and potential treatments.

Principal Investigator

Amy M. Wetherby, PhD, Florida State University

Consortium Lead Investigators

Michael Alessandri, PhD, University of Miami

Alice S Carter, PhD, University of Massachusetts Boston

Emily Feinberg, ScD CPNP, Boston University School of Medicine

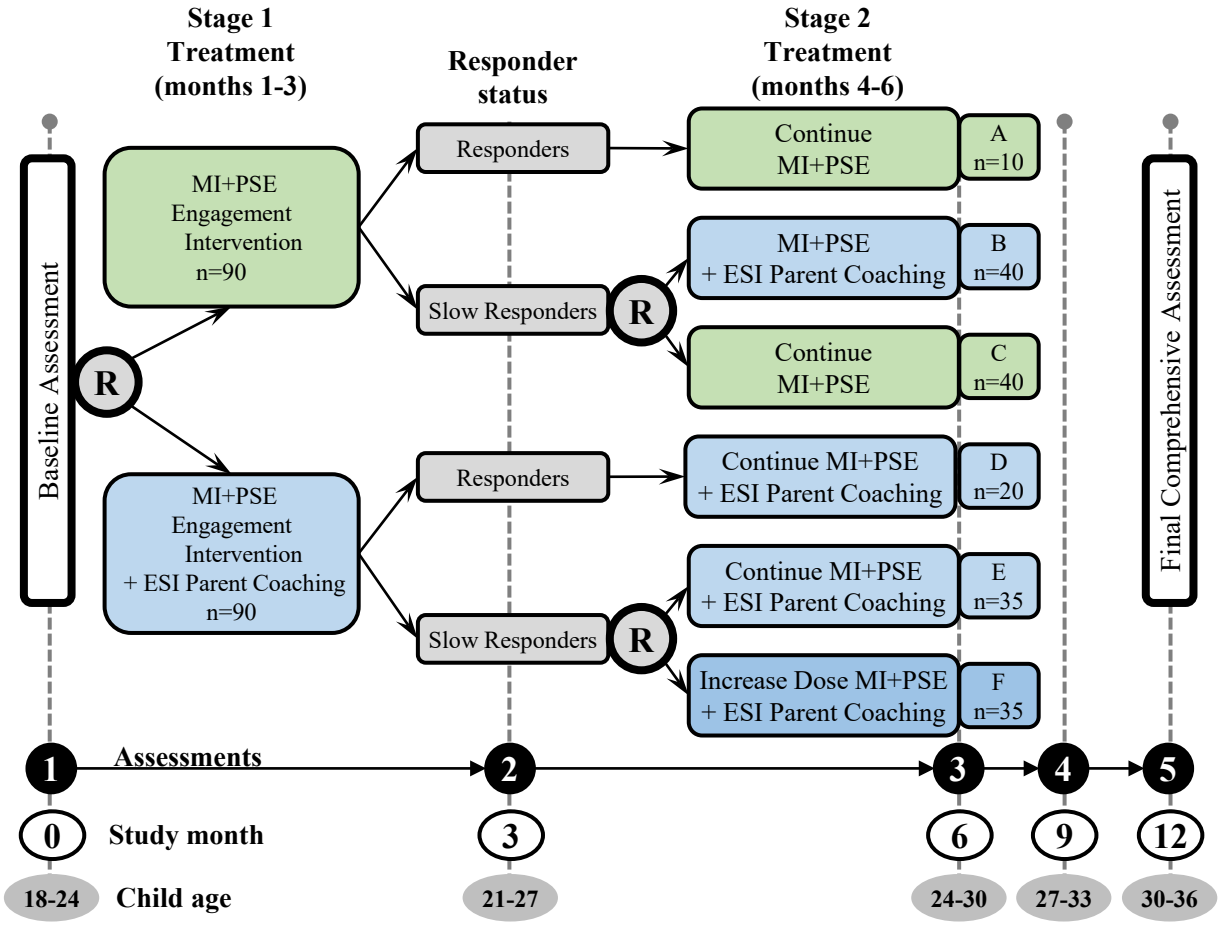
Lisa Croen, PhD, Kaiser Permanente

Blend Clinical Effectiveness and Implementation Research Designs

Study individual and combined effects of a bundle of evidence-based interventions in real world settings:

- **Engage families** to access resources and support when they first learn their child has signs of ASD using an evidence-based intervention that integrates motivational interviewing and problem-solving education (**MI+PSE**).
- **Coach families** to embed evidence-based intervention strategies for toddlers with ASD in everyday activities using the *Early Social Interaction* (**ESI**) model.
- **Infuse mobile technology** using the **Autism Navigator®** collection of web-based courses and tools.
- Develop a new **workforce** of community members—**family navigators**—who can address social determinants of health AND provide rapid, available autism treatment.

Figure 1. Phase 1: SMART of MI+PSE Engagement Intervention and ESI Parent Coaching



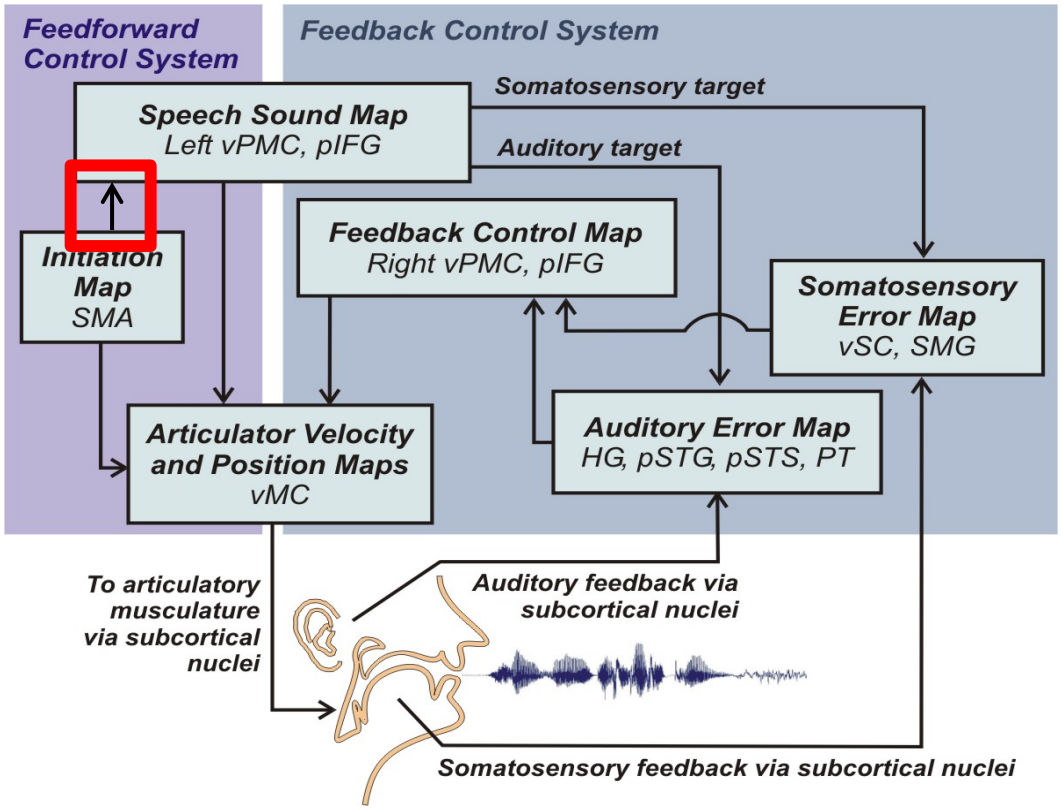
Note. **MI** = **M**otivational **I**nterviewing; **PSE** = **P**roblem-**S**olving **E**ducation; **ESI** = **E**arly **S**ocial **I**nteraction Parent Coaching Model; **R** = **R**andom assignment; **SMART** = **S**equential **M**ultiple **A**ssignment **R**andomized **T**rial

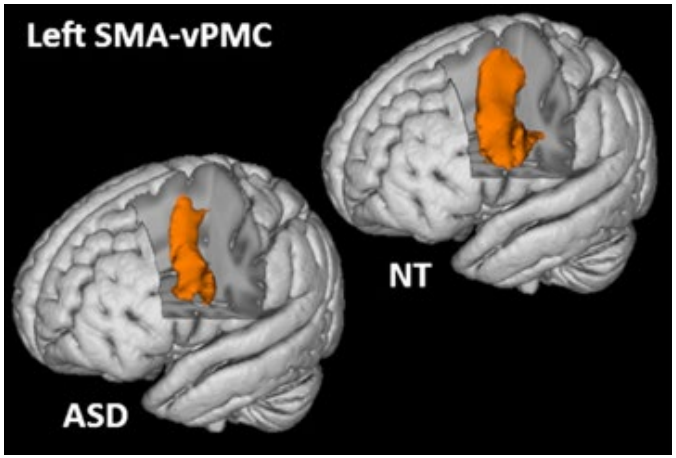
Neural Anomalies in the Speech Network of Individuals with Autism

Frank Guenther

Professor
Department of Speech, Language, & Hearing Sciences
Sargent College of Health & Rehabilitation Sciences

DIVA Model of Speech Production



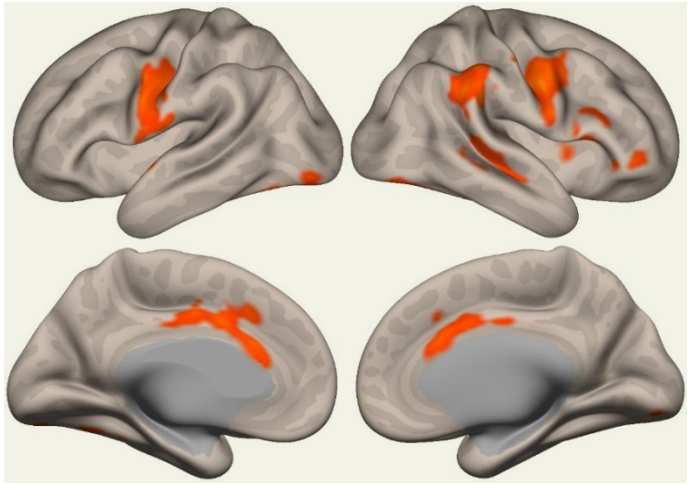


Peeva et al. (2013): Used diffusion-weighted MRI to identify impaired white matter in speech initiation circuit in ASD.

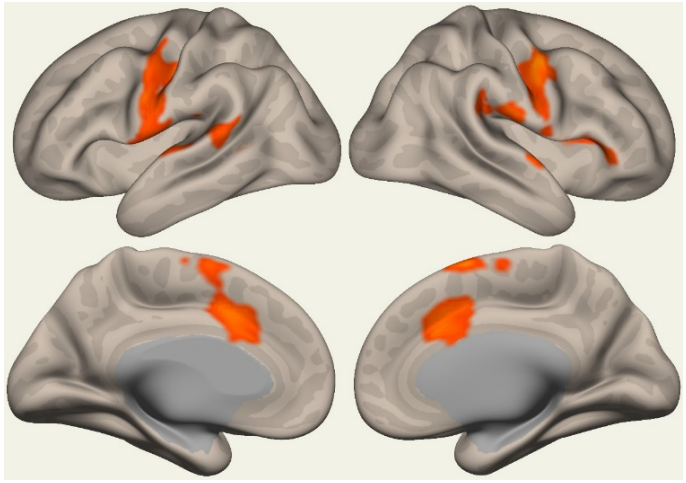
The model provides a framework for interpreting neural anomalies in the speech network of disordered populations.

Brain activity during single word production task:

Control (n = 14)

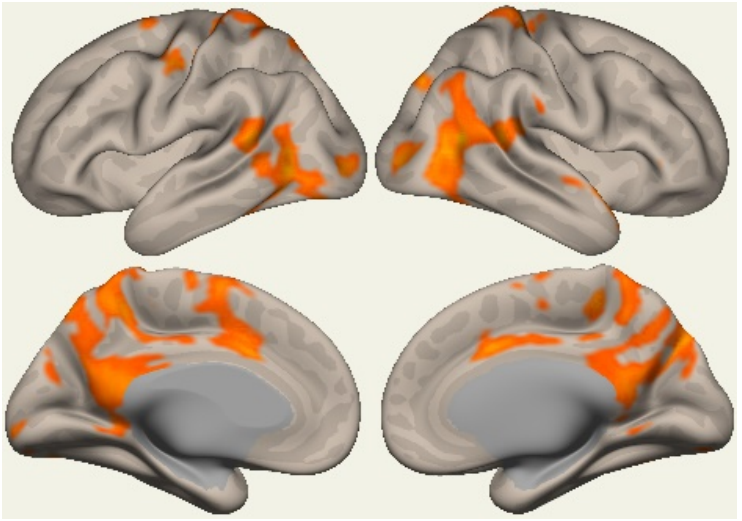


ASD (n = 15)



Speech activity in ASD not significantly different from controls at the group level, but ASD participants show more variable individual-subject activity patterns.

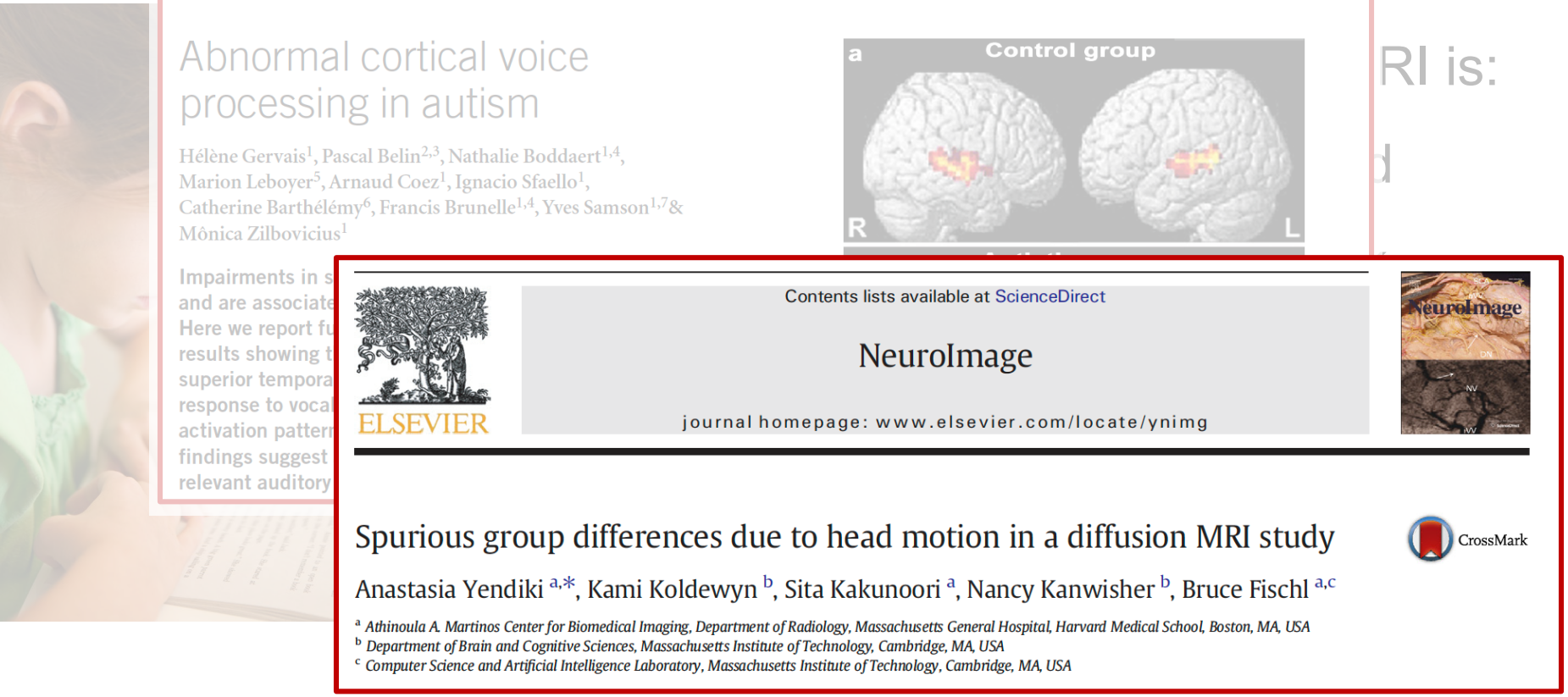
Minimally Verbal ASD Participant



One Brain at a Time: How Advances in Single-subject fMRI Analysis can help Unmask Language Impairments in Autism

Tyler Perrachione

Assistant Professor
Speech, Language and Hearing Sciences
Sargent College



BRIEF COMMUNICATIONS

Abnormal cortical voice processing in autism

Hélène Gervais[1], Pascal Belin[2,3], Nathalie Boddaert[1,4], Marion Leboyer[5], Arnaud Coez[1], Ignacio Sfaello[1], Catherine Barthélémy[6], Francis Brunelle[1,4], Yves Samson[1,7]& Mônica Zilbovicius[1]

Impairments in s
and are associate
Here we report fu
results showing t
superior tempora
response to vocal
activation patter
findings suggest
relevant auditory

RI is:

Contents lists available at ScienceDirect

NeuroImage

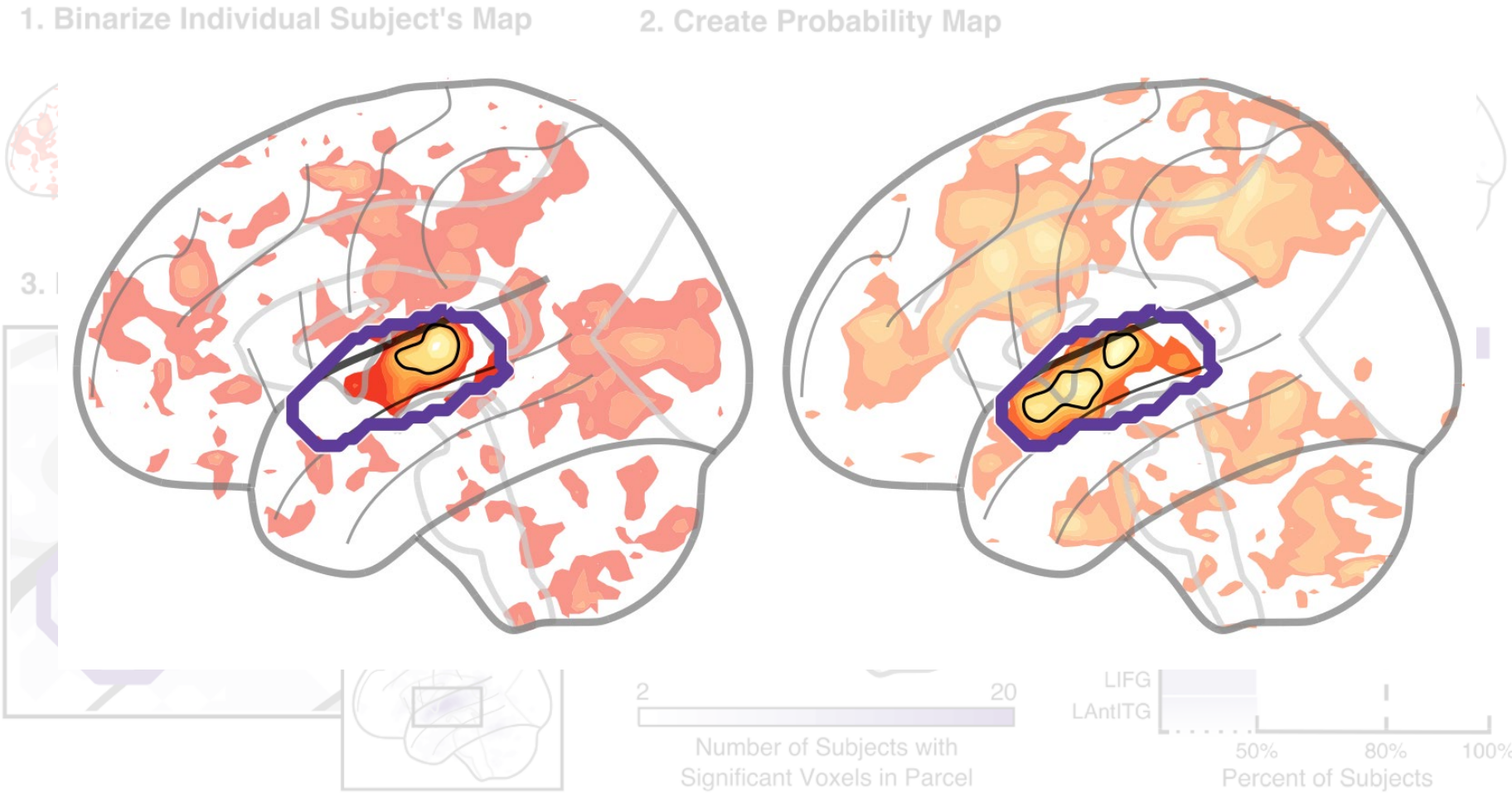
journal homepage: www.elsevier.com/locate/ynimg

Spurious group differences due to head motion in a diffusion MRI study

Anastasia Yendiki [a,*], Kami Koldewyn [b], Sita Kakunoori [a], Nancy Kanwisher [b], Bruce Fischl [a,c]

[a] Athinoula A. Martinos Center for Biomedical Imaging, Department of Radiology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA
[b] Department of Brain and Cognitive Sciences, Massachusetts Institute of Technology, Cambridge, MA, USA
[c] Computer Science and Artificial Intelligence Laboratory, Massachusetts Institute of Technology, Cambridge, MA, USA

A new approach to individualized fMRI:
Group-Constrained Subject-Specific Analysis



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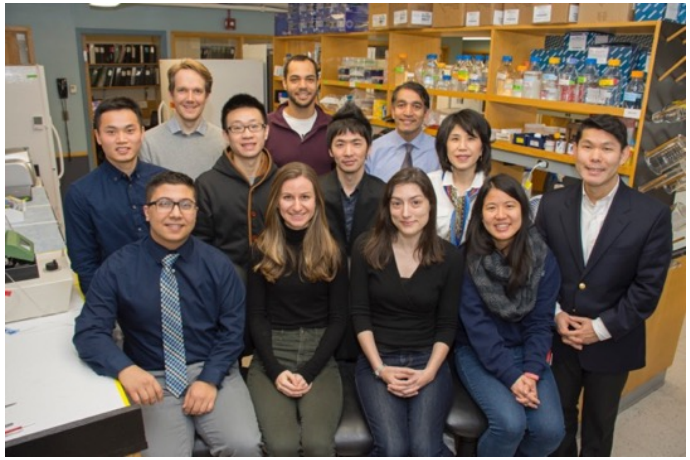
Microglia as Therapeutic Target of Maternal Immune Activation-associated ASD

Removing microglia normalizes neurodevelopmental abnormality in maternal immune activation offspring mouse model



Tsuneya Ikezu, MD, PhD

Professor

Departments of Pharmacology and Experimental Therapeutics and Neurology, Boston University School of Medicine

Boston University Office of the Vice President and Associate Provost for Research

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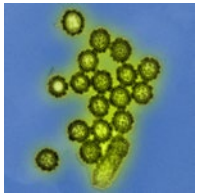
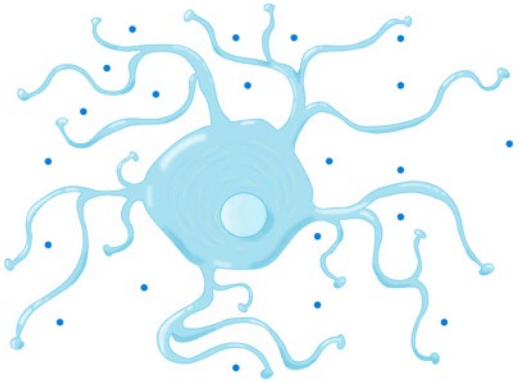
Immune response to the environmental factor may be a key to solve the mystery of Autism Spectrum Disorders (ASD)

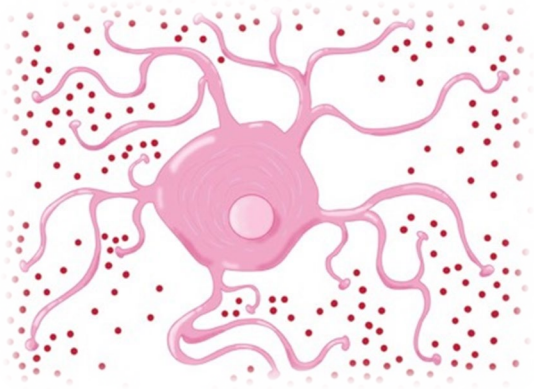
Fetal microglia, immune cells in the brain, respond to immune stimuli and change their function



Normal microglia



MIA microglia



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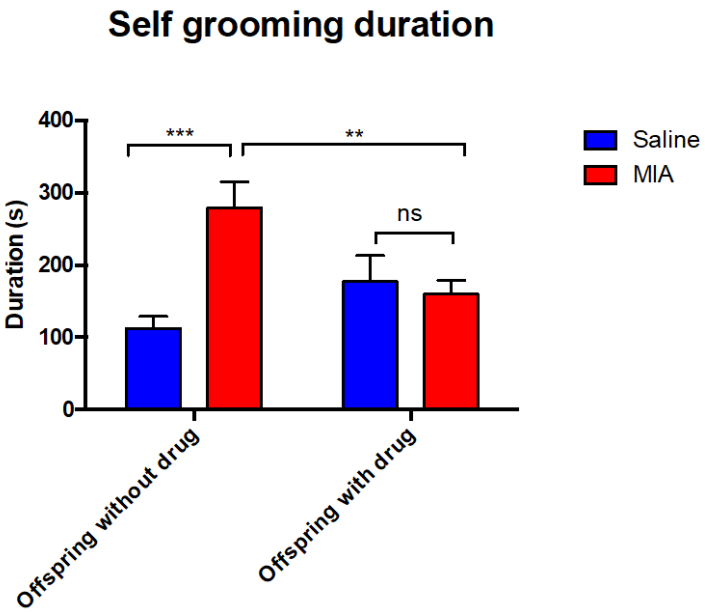
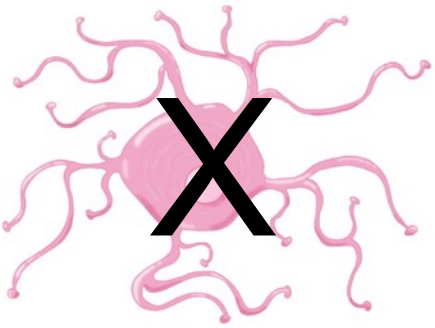
Removing microglia, brain immune cell, normalizes ASD like behavioral abnormality

Offspring from Co
or MIA mother on





Removing offspring microglia

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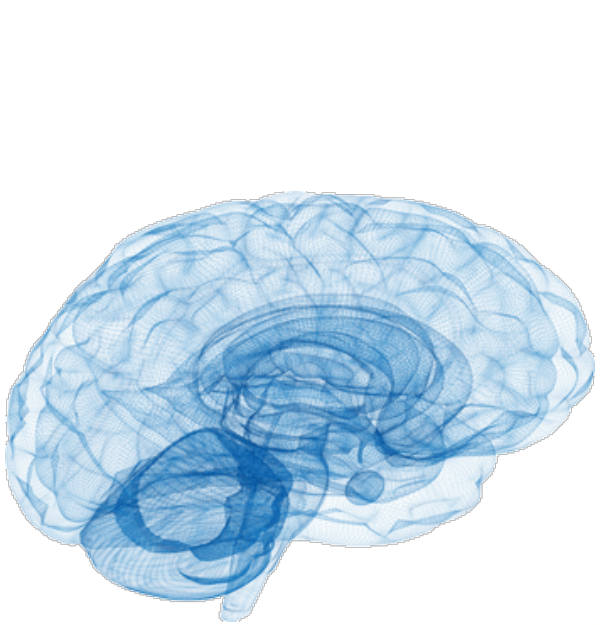
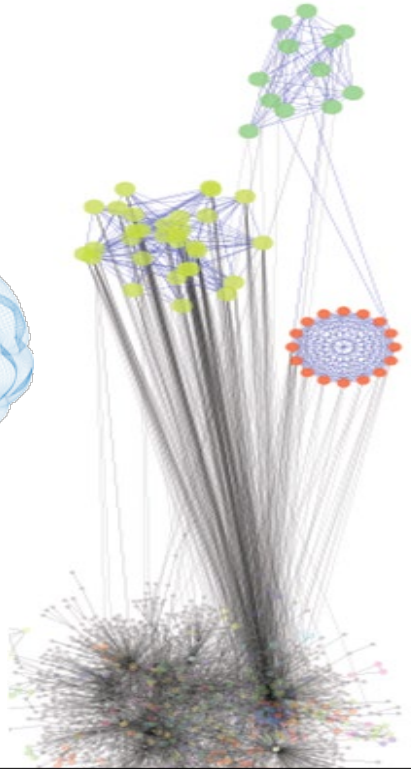
Mapping the Landscape of Brain Protein Networks Altered in Autism

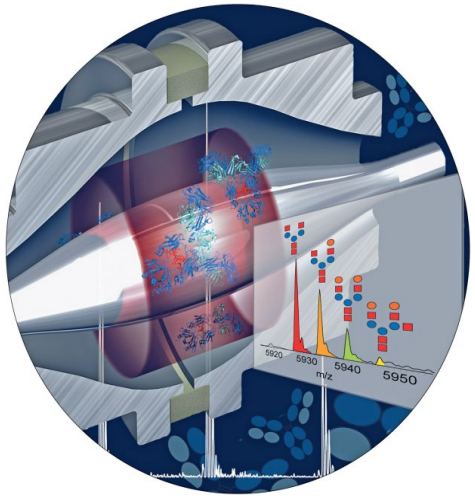
Andrew Emili

Professor of Biochemistry and Biology Director, Center for Network Systems Biology

Mapping the landscape of brain protein networks altered in Autism







"A hidden connection is stronger than an obvious one"

- Heraclitus of Ephesus 535–475 BC

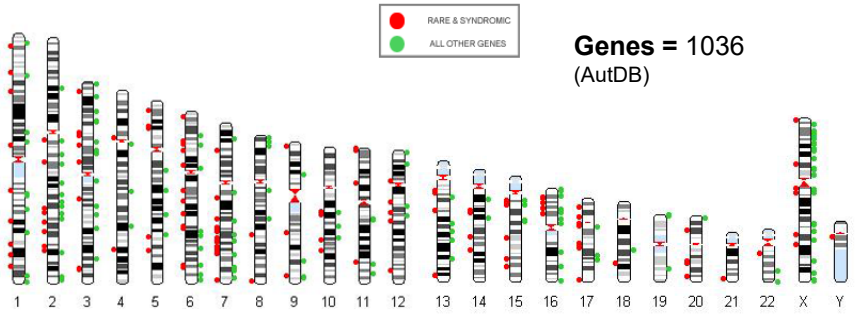
CNSB
Center for Network Systems Biology

Andrew Emili

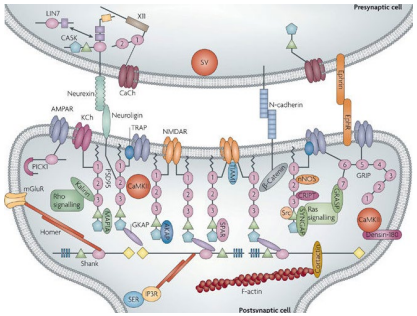
Boston University (Biology & Biochemistry)

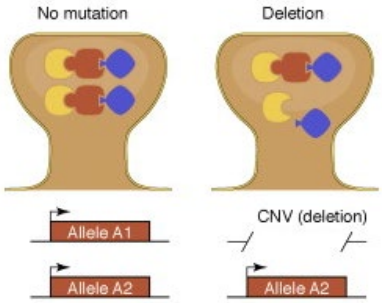
Research on Tap: Autism - Boston - November 2, 2018

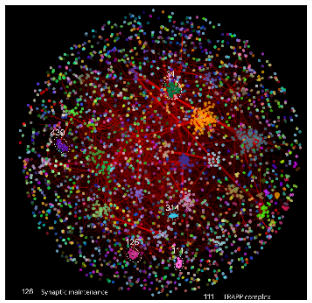
Genes, Mutations, Networks, Dysfunction

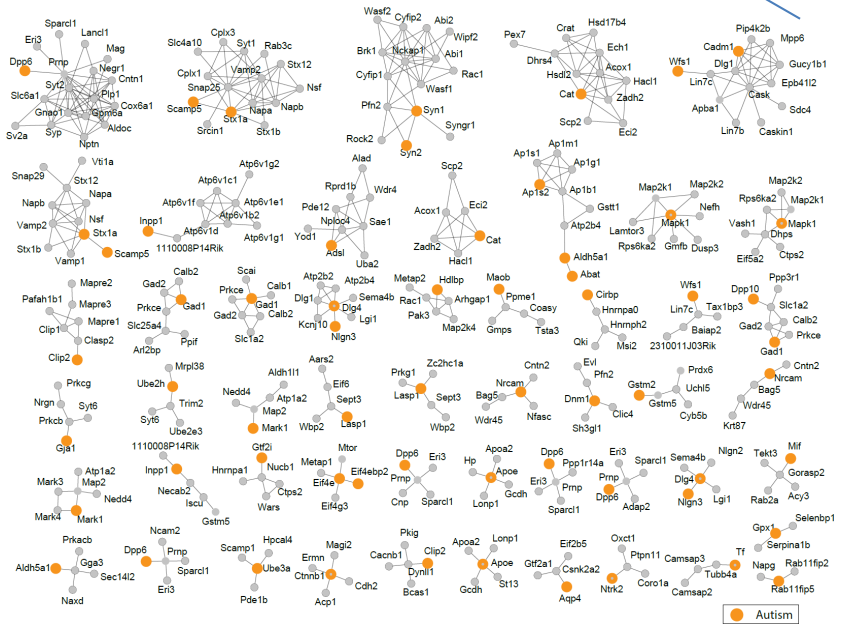


Genes = 1036
(AutDB)

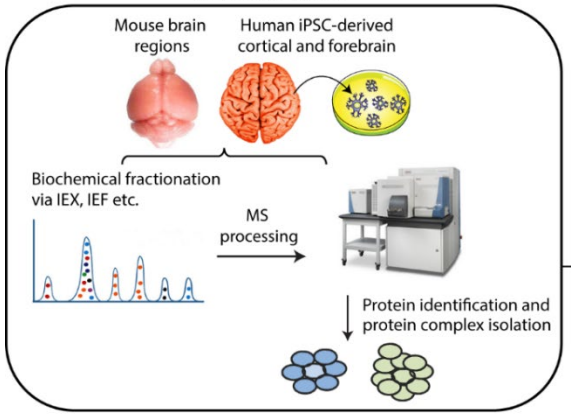




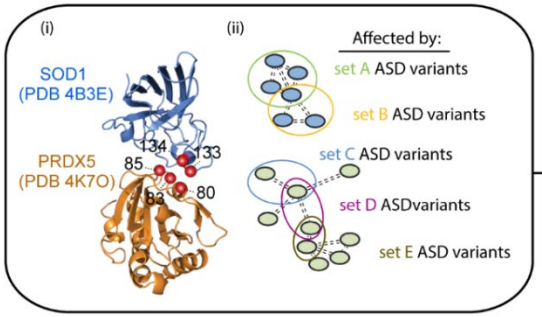




BP/MS complex from
mouse brain (Aim 1)



3D structural interactome models
and impact of ASD mutations (Aim 2)



Loss of PPI due to ASD mutations

Validation of prioritized PPIs and its
relevance to ASD and NDs (Aim 3)

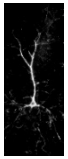
Development of Network Disruptions in Autism

Basilis Zikopoulos

Assistant Professor

Department of Health Sciences, SAR

HUMAN ΣΥΣΤΕΜS NEUROΣCIENCE ΛAB



Supported by grants from NIMH and Autism Speaks

NIMH National Institute of Mental Health

AUTISM SPEAKS

Tissue donors and families

Autism Tissue Program
NICHD Brain and Tissue Bank for Developmental Disorders
Institute for Basic Research in Developmental Disabilities (IBR)
National Disease Research Interchange (NDRI)

Boston University Office of the Vice President and Associate Provost for Research

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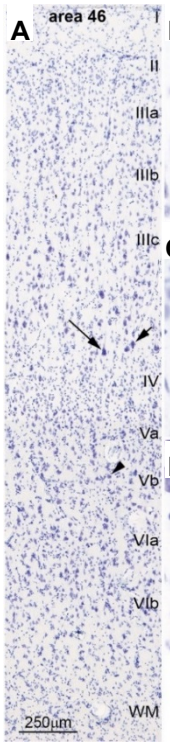
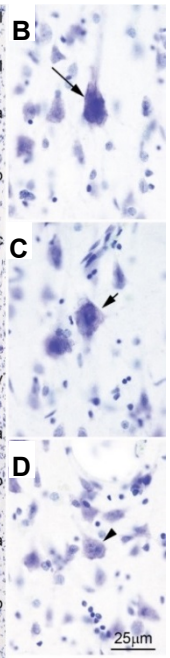
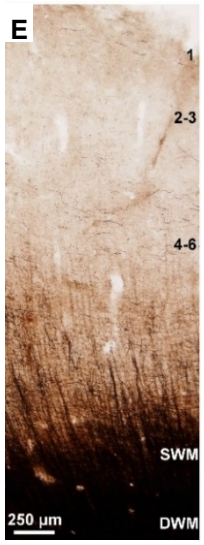
Research on Tap: Current Research on Autism at Boston University: From Cells to Society

Cytoarchitecture

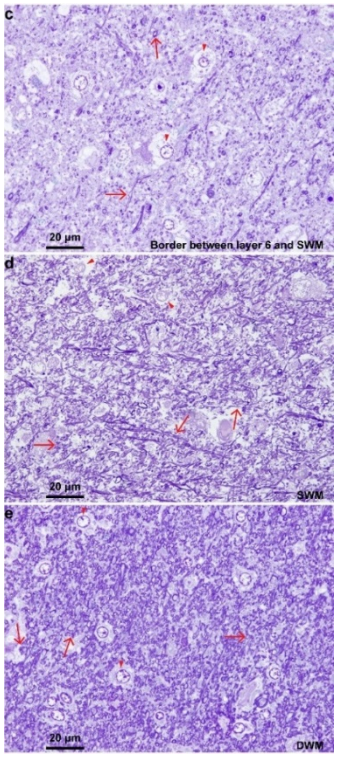


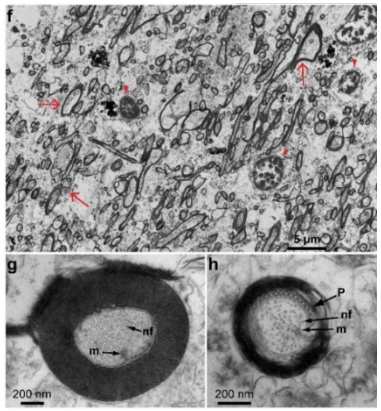


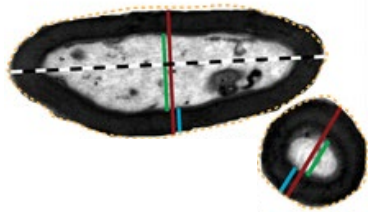
Myeloarchitecture



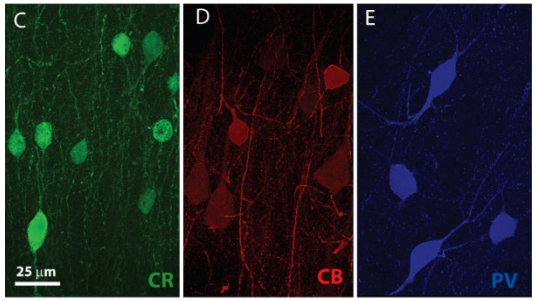
Excitatory pathways







Inhibitory circuits



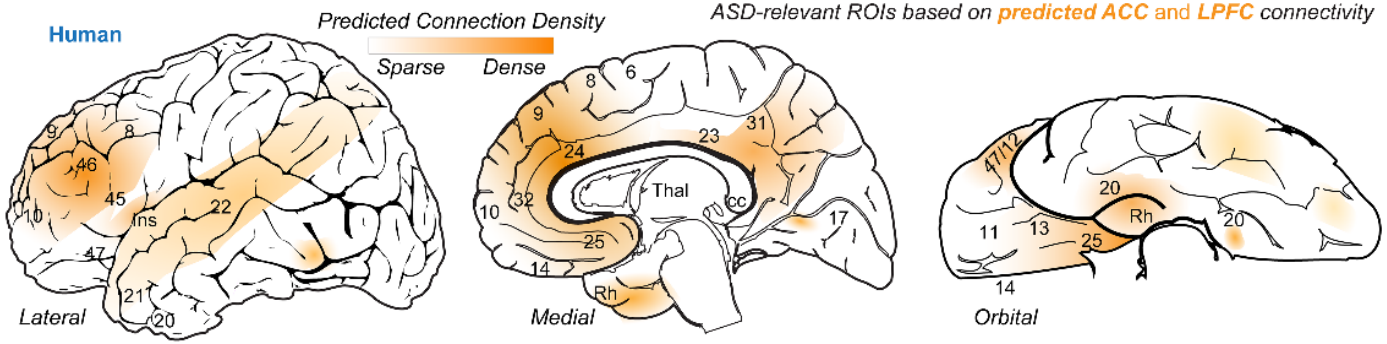
Calretinin
Innervate other inhibitory neurons
Dis-inhibitory effect

Calbindin
Distal innervation
Modulatory inhibition

Parvalbumin
Proximal innervation
Strong inhibition

- Disruption of key developmental processes:
  - Changes in density, myelination, growth, and branching of excitatory axons
  - Changes in density of inhibitory neurons

Cortical networks



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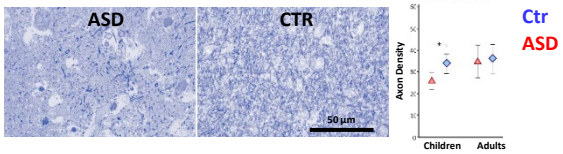
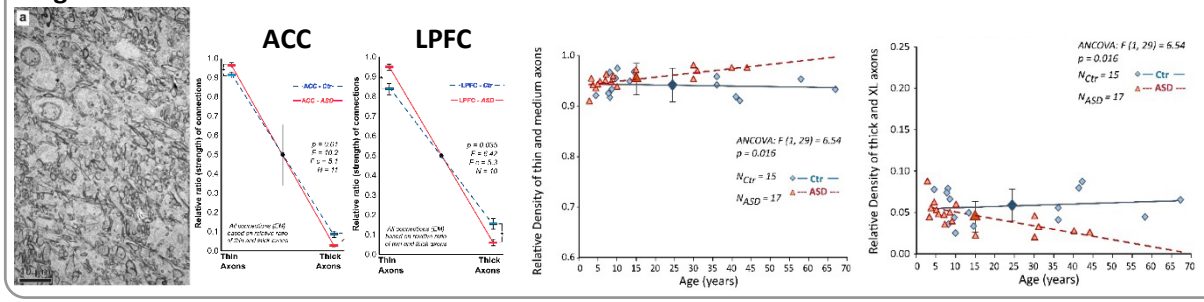
Axon pathology is at the core of atypical connectivity in ASD

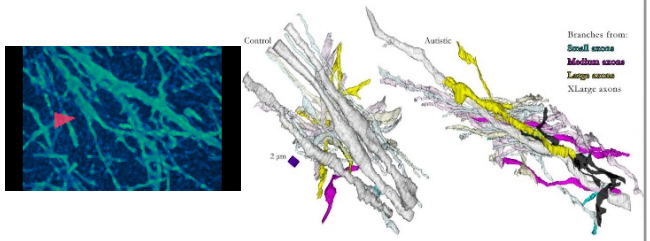
Fewer myelinated axons in children with ASD



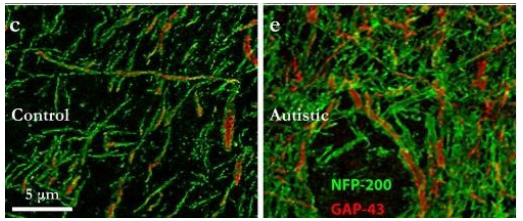
Development of excessive connectivity within the frontal lobe and progressive weakening of long-range cortical connections



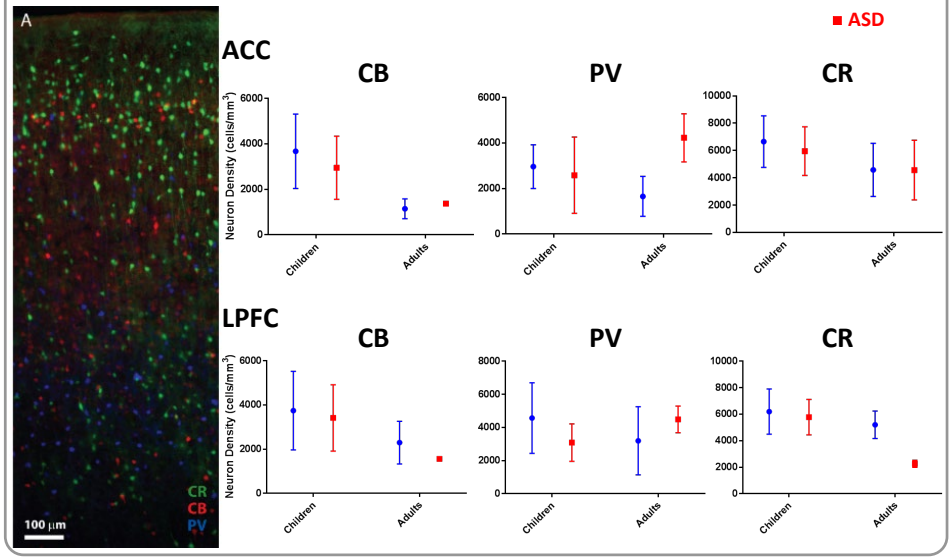
Increased axonal branching in the frontal lobe



Increased axon growth in the frontal lobe



Cortical inhibition changes in ASD



Disruption in the balance of excitation/inhibition scrambles neural communication in ASD