



National Institute
of Mental Health

OFFICE OF
AUTISM RESEARCH
COORDINATION
NATIONAL INSTITUTES OF HEALTH

Office for Research on
Disparities and Global Mental Health

AUTISM IN GIRLS AND WOMEN

A PANEL DISCUSSION

TUESDAY, SEPTEMBER 19, 2017 • 1:00 PM - 3:00 PM

NEUROSCIENCE CENTER (NSC) • 6001 EXECUTIVE BLVD • ROOM 7102

Event will also be available live on videocast.nih.gov



Zoe Gross



Kevin Pelphey, Ph.D.



Pamela Ventola, Ph.D.



ABOUT THE SPEAKERS



KEVIN PELPHREY, PH.D.

*Carbonell Family Professor
Director, Autism and Neurodevelopmental Disorders Institute
at George Washington University and Children's National
Medical Center*

Dr. Kevin Pelphrey is the Carbonell Family Professor and Director of the Autism & Neurodevelopmental Disorders Institute at George Washington University (GW) and Children's National Health System (CNHS) in Washington, DC. The Institute serves as a focal point for translational research and comprehensive clinical services for people living with Autism Spectrum Disorder (ASD). His program of research investigates the brain basis of neurodevelopmental disorders to develop biologically-based tools for detection, stratification, and individually tailored treatments. Dr. Pelphrey is also the Principal Investigator of the NIH ACE-Multimodal Developmental Neurogenetics of Females with Autism network. This Network has generated a comprehensive, multi-level (gene-brain-behavior) data from large and diverse cohorts of young women and men with ASD. Dr. Pelphrey joined the Interagency Autism Coordinating Committee as a public member in 2015. He is the father of a son and a daughter on the autism spectrum.



PAMELA VENTOLA, PH.D.

Assistant Professor, Yale Child Study Center

Dr. Pamela Ventola is a clinical psychologist and Assistant Professor at the Yale Child Study Center. Her clinical work and research program focus on behavioral treatment for ASD, specifically, Pivotal Response Treatment (PRT). She also has a strong interest in girls and women with ASD. She has conducted several studies on sex-based differences in treatment response, and she is currently collaborating with Dr. Kevin Pelphrey on a multi-site study related to the neurogenetics of females with ASD. Dr. Ventola is heavily involved in the clinical components of this multi-site program. Additionally, she is commencing a study with Dr. Pelphrey to assess the effects of oxytocin as an enhancer of response to PRT. Evaluating sex-based differences to this combination treatment is a key aim of the new project.



ZOE GROSS

Director of Operations, Autistic Self Advocacy Network

Zoe Gross is Director of Operations at Autistic Self Advocacy Network. Previously, she worked as a special assistant at the Administration for Community Living, and as a policy analyst on Senator Tom Harkin's Health, Education, Labor and Pensions Committee staff. In 2012, Zoe created the annual Disability Day of Mourning vigil, a national, cross-disability event which commemorates the lives of disabled people murdered by their family members or caregivers.



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Recent advances in research suggest that autism spectrum disorder (ASD) presents differently in males and females.

As a result, researchers are seeking to understand the biological differences between ASD in males and females, as well as reevaluating the effectiveness of diagnostic tools and treatments for females on the autism spectrum. Meanwhile, girls and women with ASD are sharing their stories in order to increase awareness among researchers and the general public. This panel discussion will present three different perspectives on understanding ASD in girls and women.

Dr. Kevin Pelphrey will be speaking on biological aspects of sex differences in ASD, Dr. Pamela Ventola will be speaking on observable differences in phenotype between girls and boys, and Ms. Zoe Gross will be speaking on personal and community experiences related to ASD in girls and women.

1:00 PM –1:10 PM
INTRODUCTORY REMARKS

Susan Daniels, Ph.D.

*Director, Office of Autism Research Coordination,
National Institute of Mental Health*

Executive Secretary, Interagency Autism Coordinating Committee

Tamara Lewis Johnson, M.P.H., M.B.A.

*Health Scientist Administrator, Office for Research on Disparities
and Global Mental Health, National Institute of Mental Health*

Chief, Women's Mental Health Research Program

1:10 PM –1:30 PM

Kevin Pelphrey, Ph.D.

Carbonell Family Professor

*Director, Autism and Neurodevelopmental Disorders Institute
at George Washington University and Children's National
Medical Center*

1:30 PM –1:50 PM

Pamela Ventola, Ph.D.

Assistant Professor, Yale Child Study Center

1:50 PM –2:10 PM

Zoe Gross

Director of Operations, Autistic Self Advocacy Network

2:10 PM –3:00 PM
QUESTION AND ANSWER PANEL DISCUSSION

NIH Autism Center of Excellence: Girls' (Women's) Neurogenetics Network

Kevin Pelphrey & the Girls' Network Team

Autism & Neurodevelopmental Disorders Institute

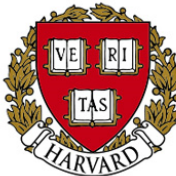
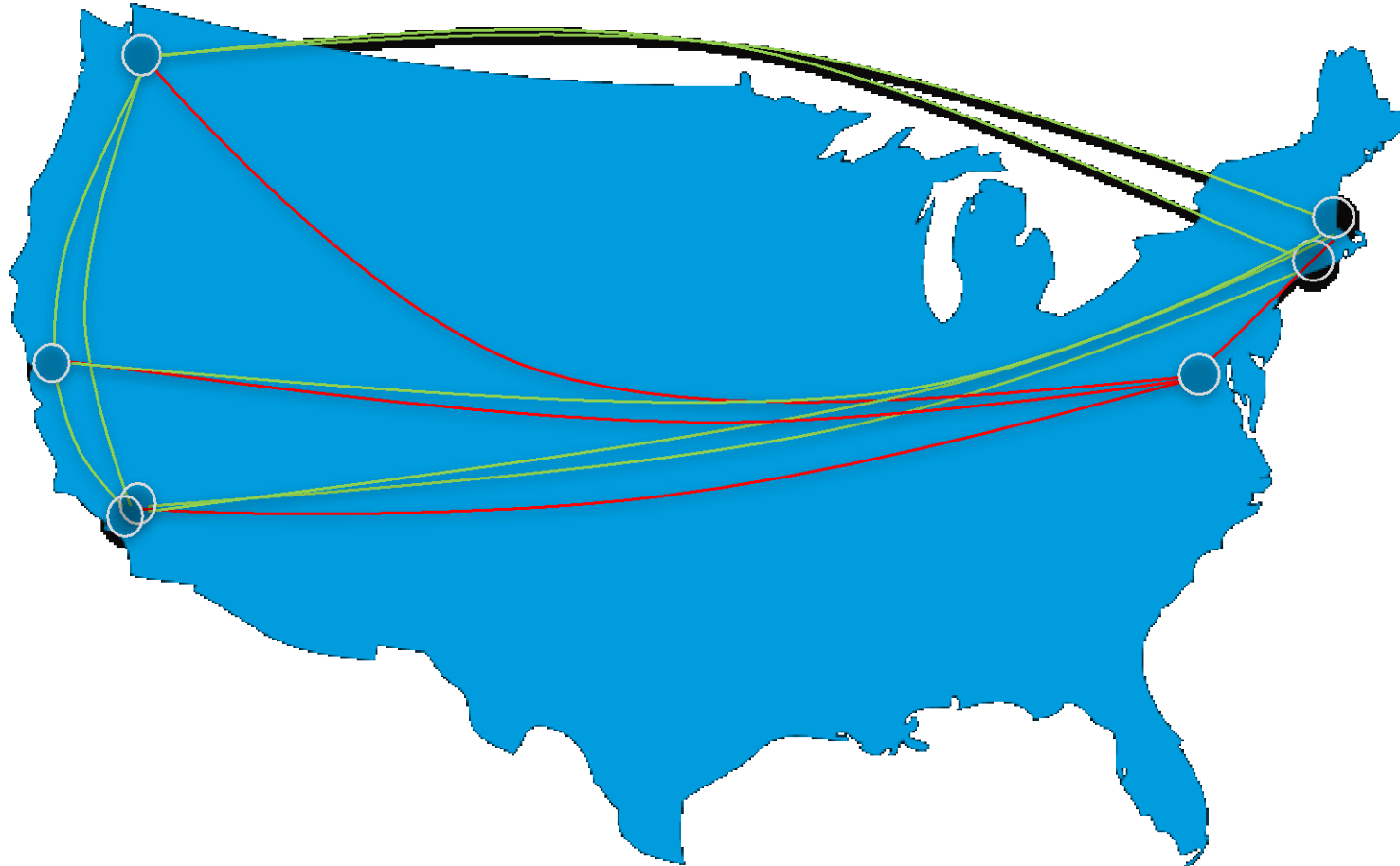
THE GEORGE
WASHINGTON
UNIVERSITY

WASHINGTON, DC



www.autism.gwu.edu

NIH Autism Center of Excellence: Girls' (Women's) Neurogenetics Network



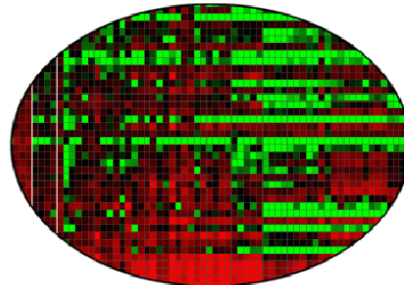
Network Aims

- 1) Identify sex differences in ASD brain development leading to gender specific biomarkers to inform treatment selection & response.**
- 2) Bridge DNA sequence and brain development.
- 3) Relate neural signatures to behavior and genetics (structure & expression) to predict behavioral trajectories.
- 4) Collaborate with ASD self-advocates / participants to evaluate the experiential validity of our findings.

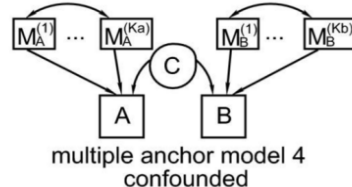
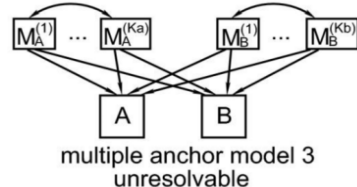
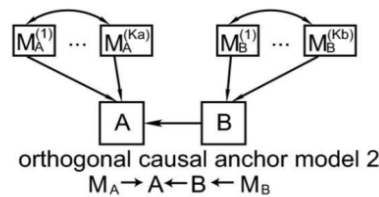
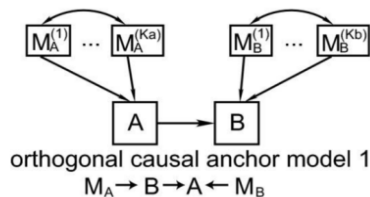
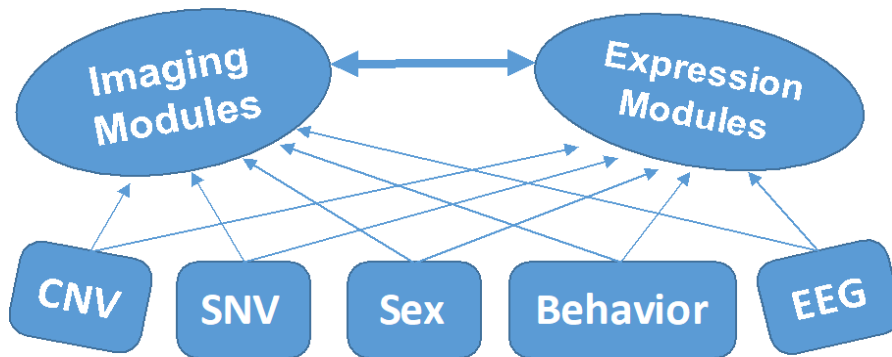
Systems Biology Approach



Neuroimaging Modules
(T1+ T2)



Gene Expression Modules

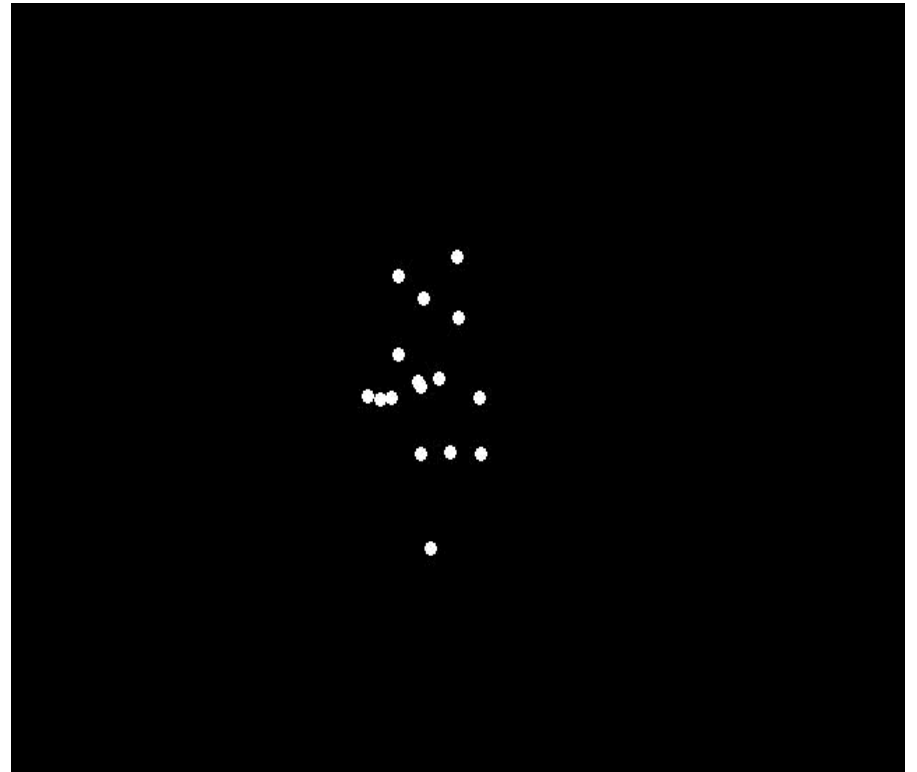
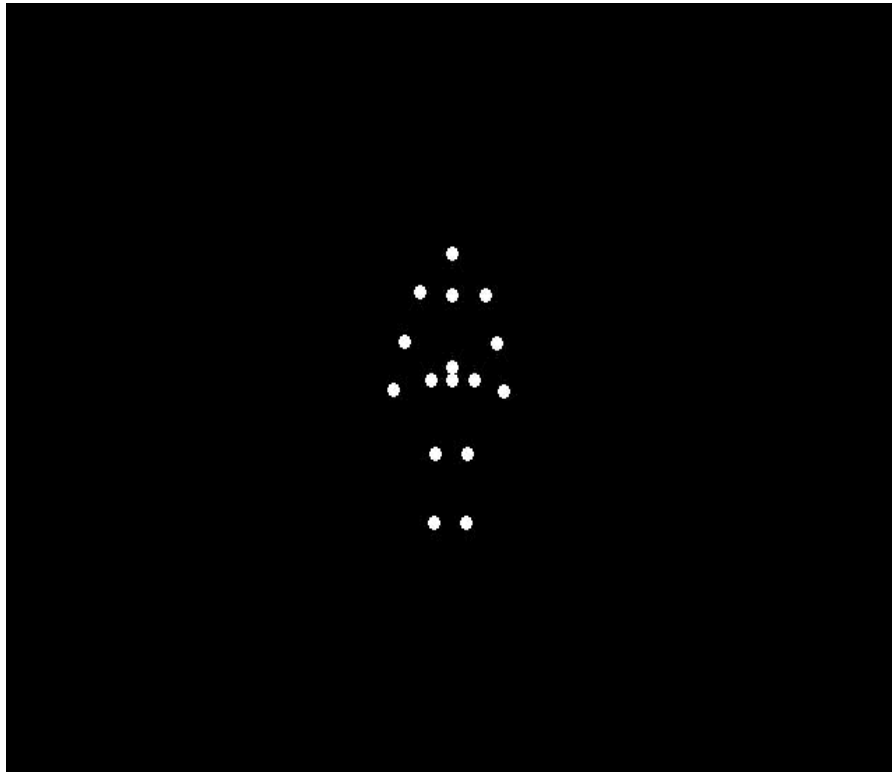


1. Apply WGCNA to imaging and expression to reduce dimensionality, define and characterize modules

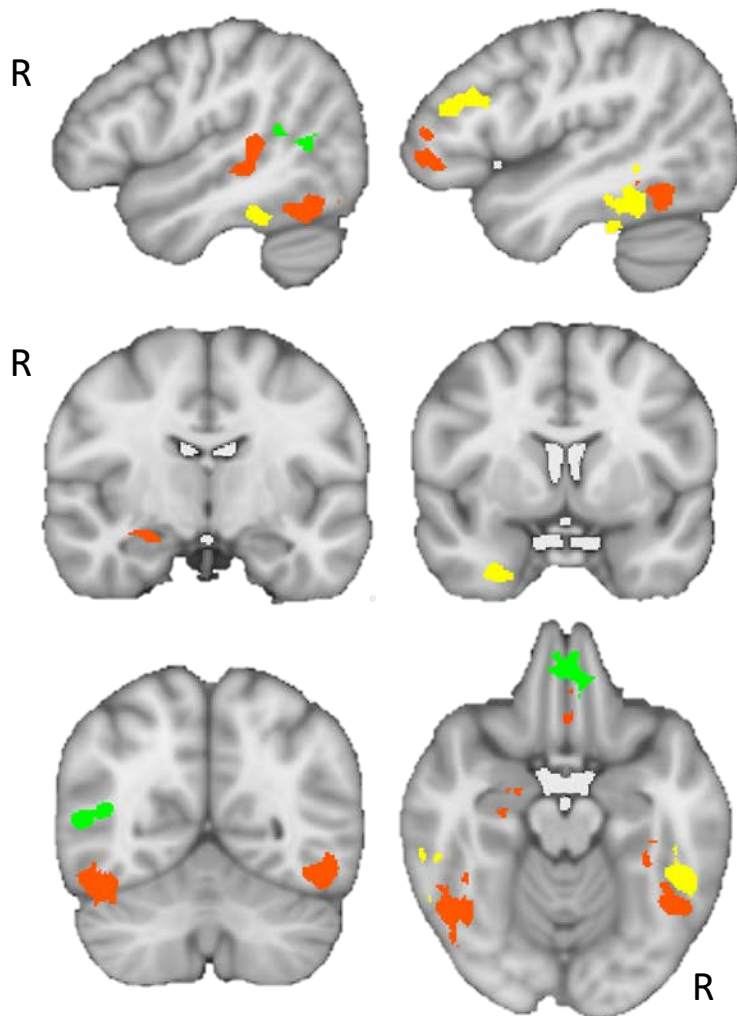
2. Identify associations between endophenotypes and between SNV, CNV, sex and endophenotypes

3. Use network edge orientation to fit relationships to a model to identify causal versus reactive relationships

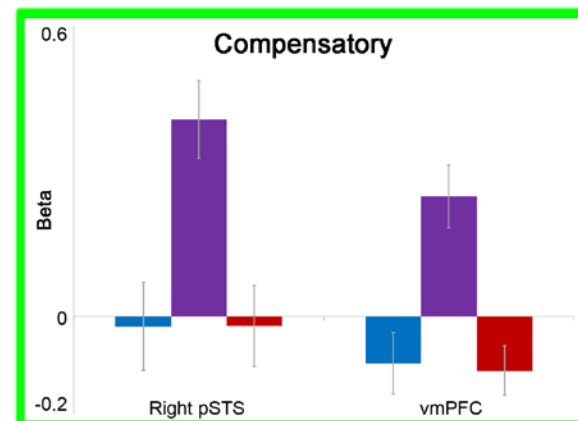
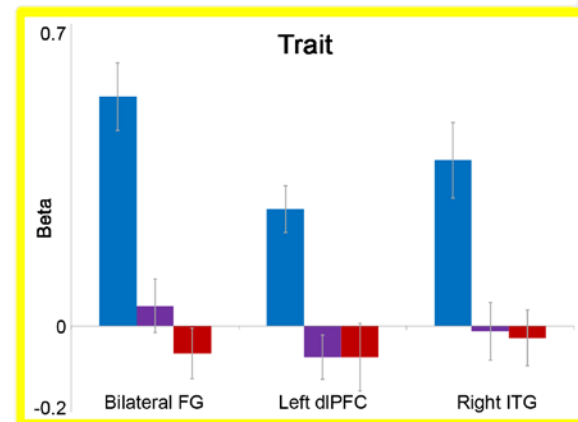
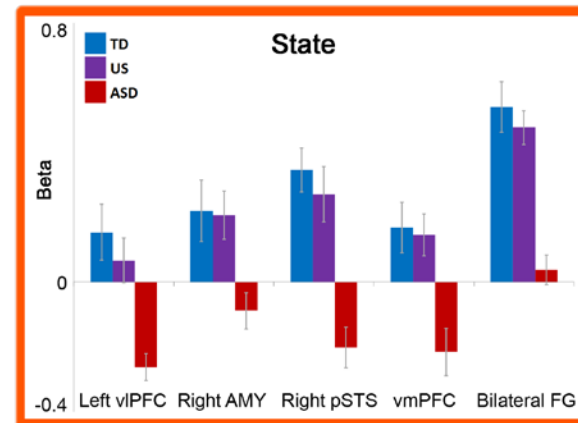
Social vs. Non-Social Motion



Kaiser et al. (2010) *Proceedings of the National Academy of Sciences*



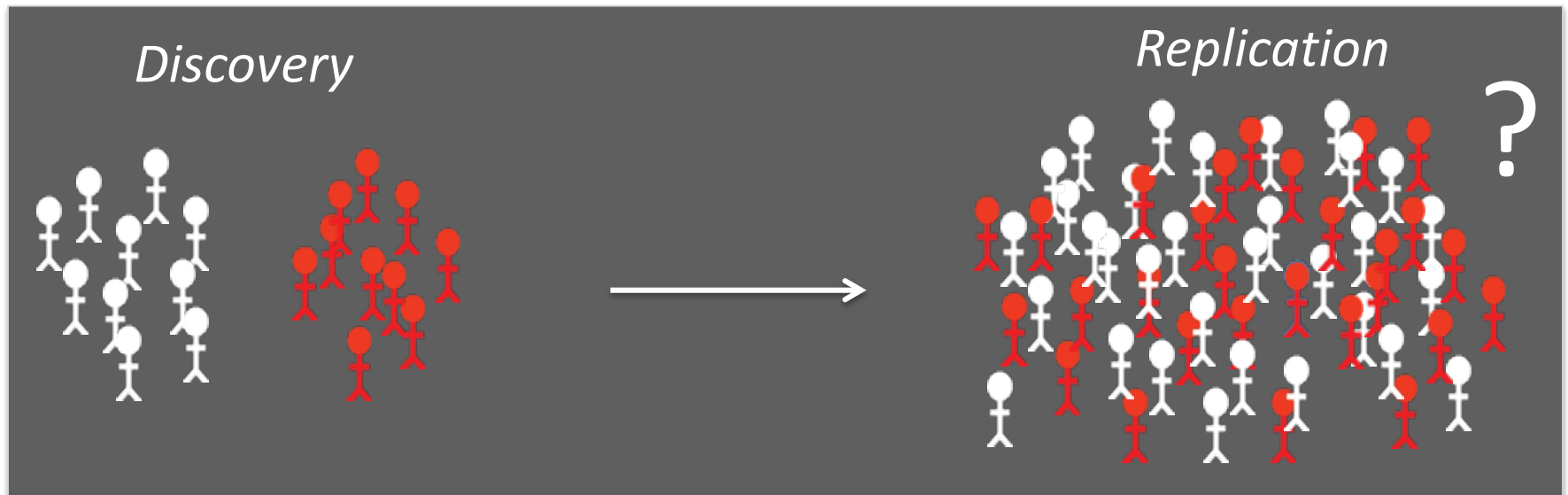
- State: ASD < TD & ASD < US
- Trait: US < TD & ASD < TD
- Compensatory: US > TD & US > ASD



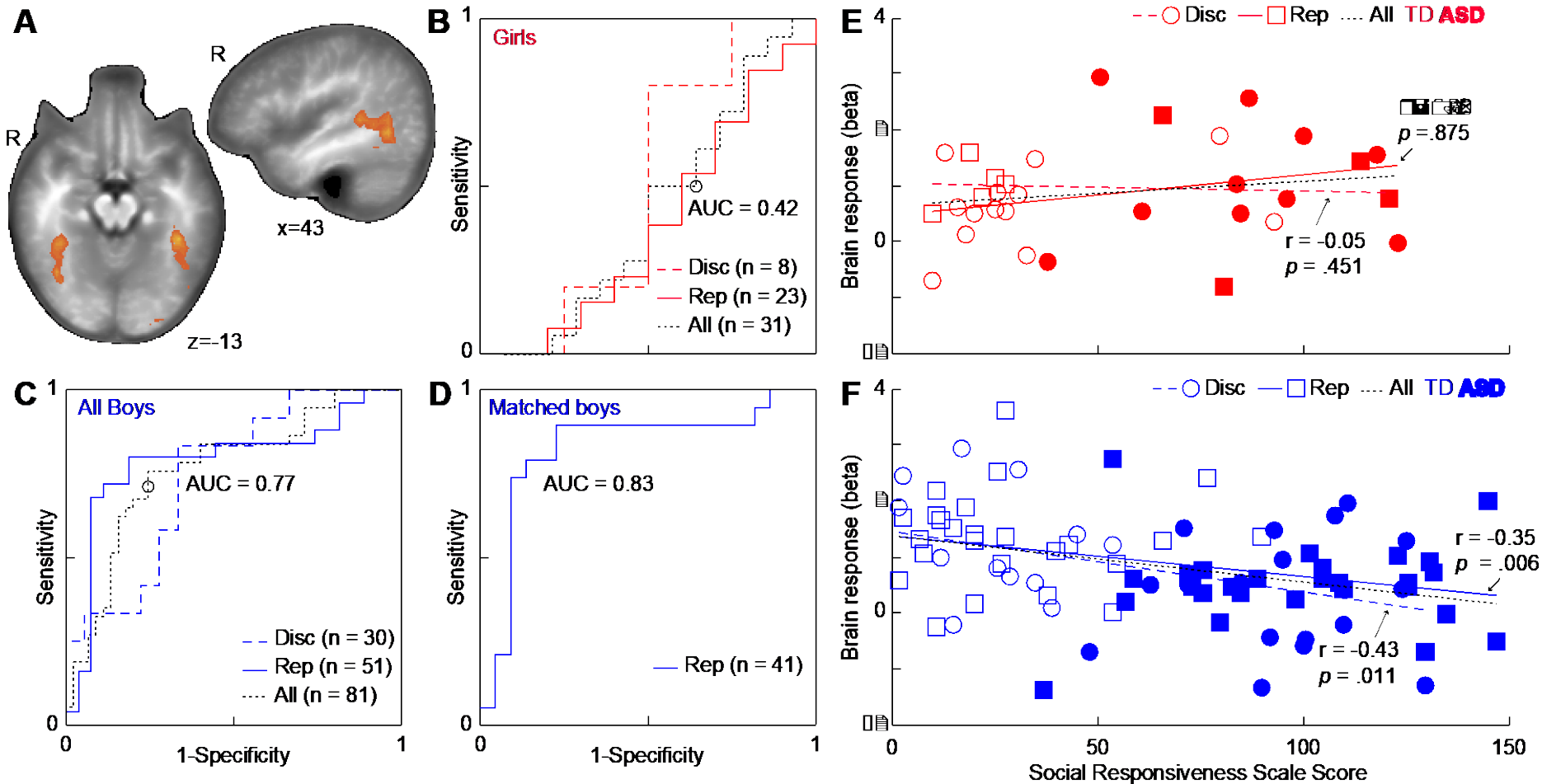
Informative at the level of the individual child?



Malin Björnsdotter, PhD



Björnsdotter et al., *JAMA: Psychiatry*, 2016

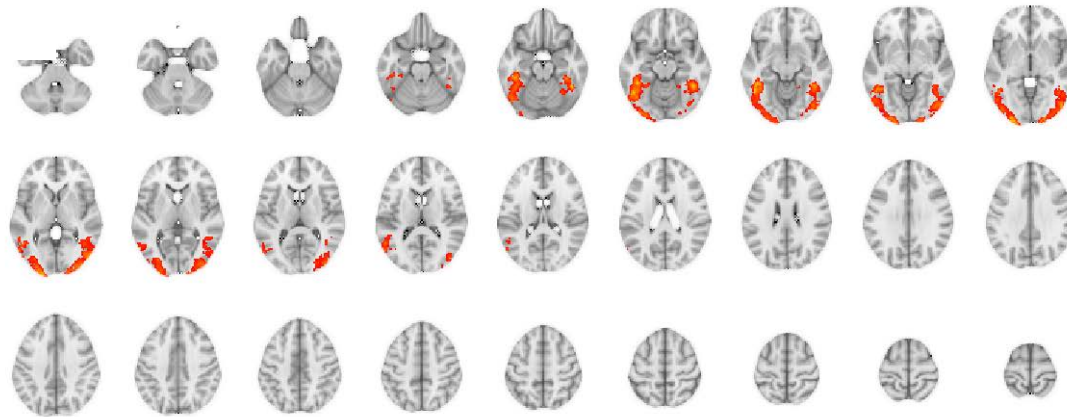


Björnsdotter et al., *JAMA: Psychiatry*, 2016



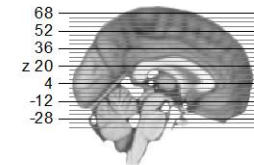
Allison Jack, PhD

ASD ♀ (n = 46)

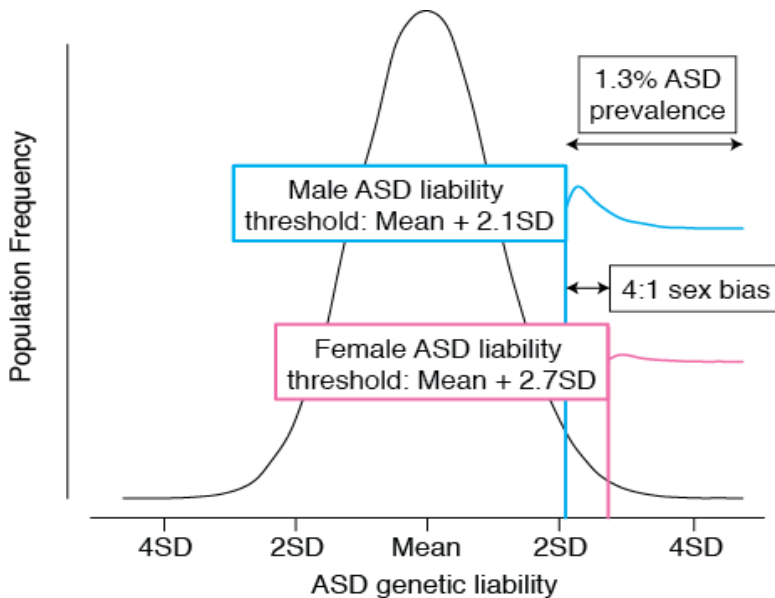
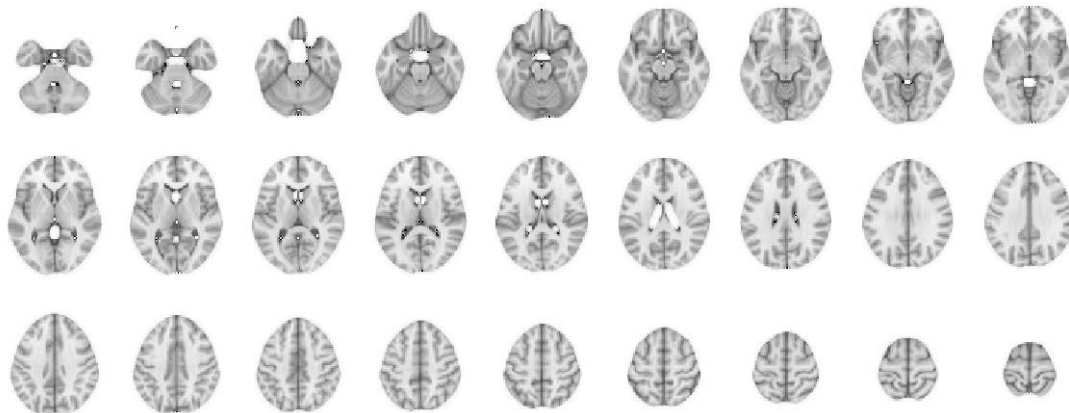


Displayed in neurological convention
(right hemisphere displayed on right).

z = 2.3  5.0
Cluster corrected $p < .001$

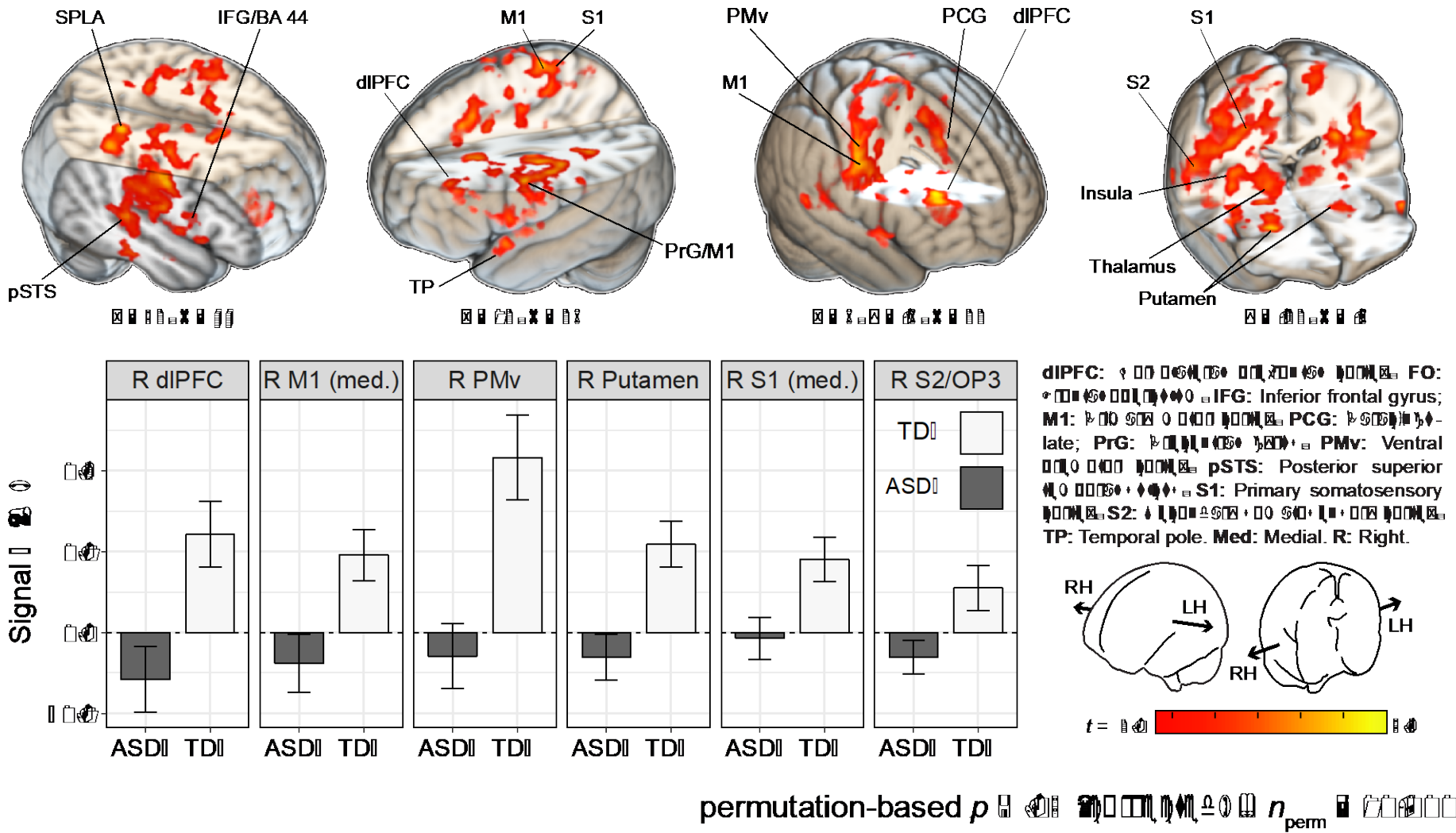


ASD ♂ (n = 48)



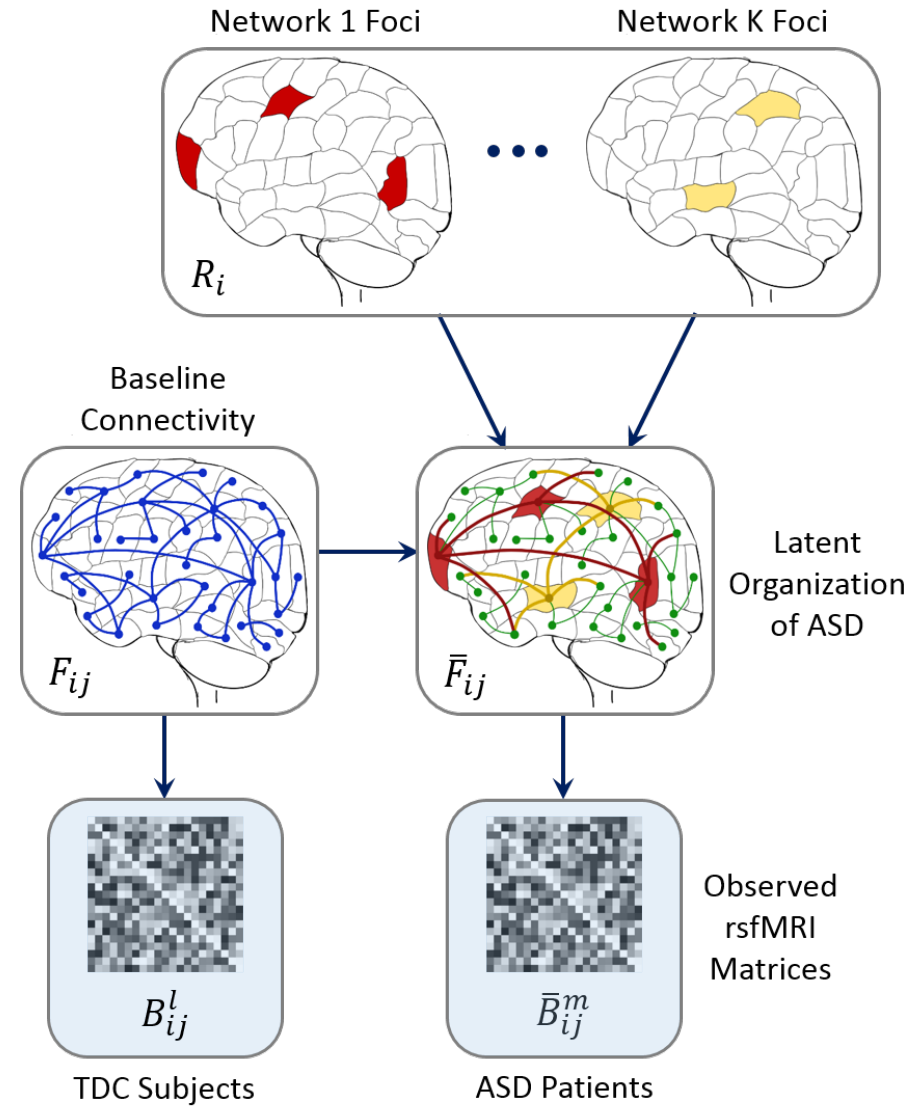
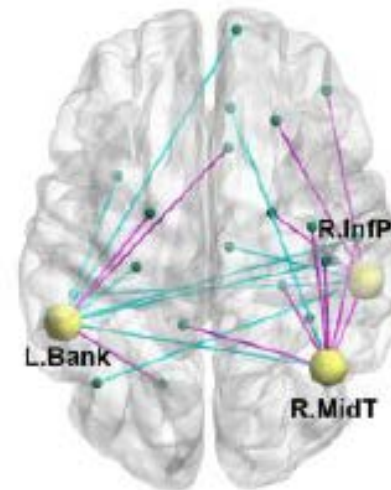
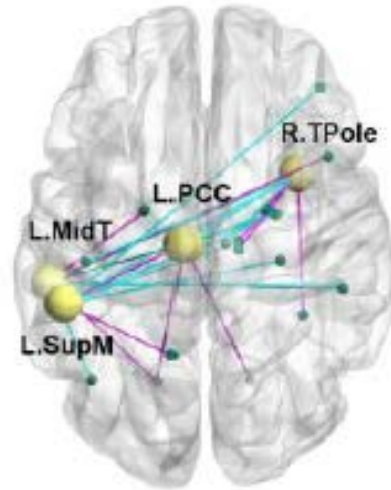
Group differences in BIO > SCRAM, controlling for FSIQ, age, site, and SRS.

TD > ASD





Archana Venkataraman, PhD



Boys – Network to Construct mapping

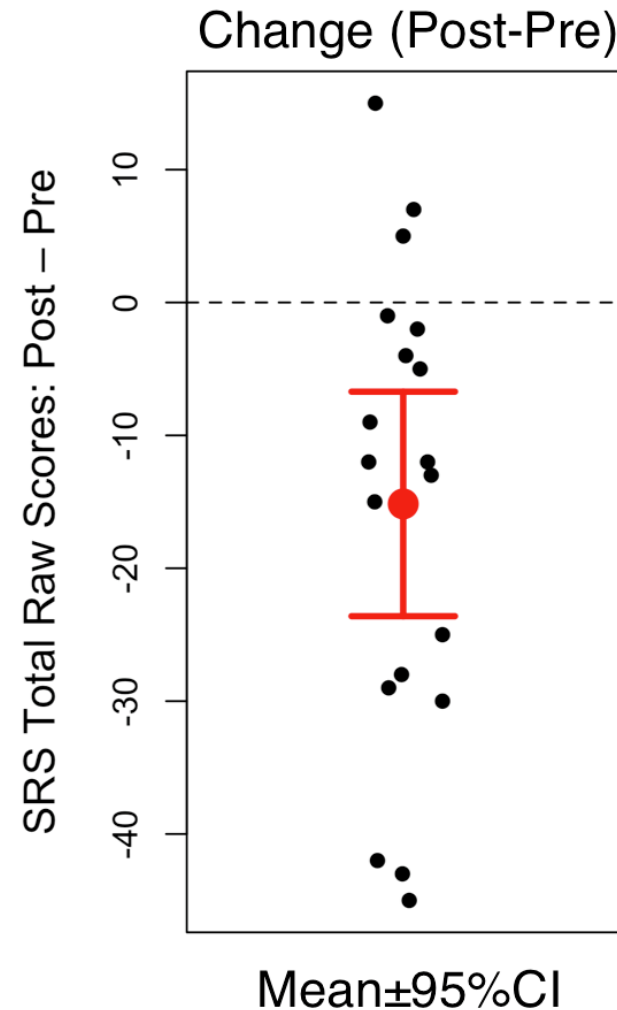
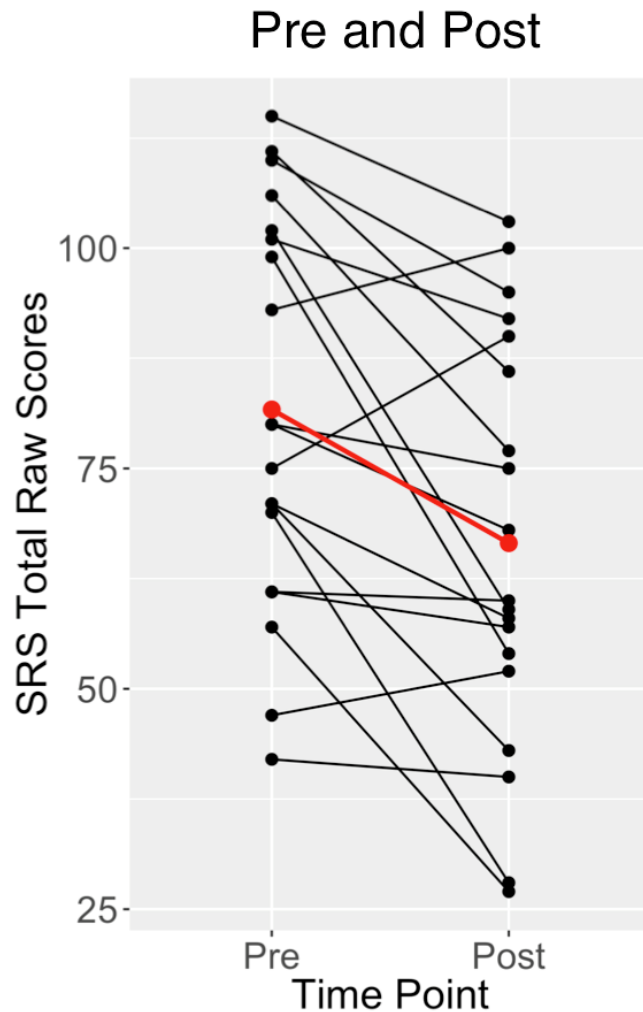


Problem: Lack of predictive autism biomarkers perpetuates the *status quo* of imprecise treatments, wasted time & resources.

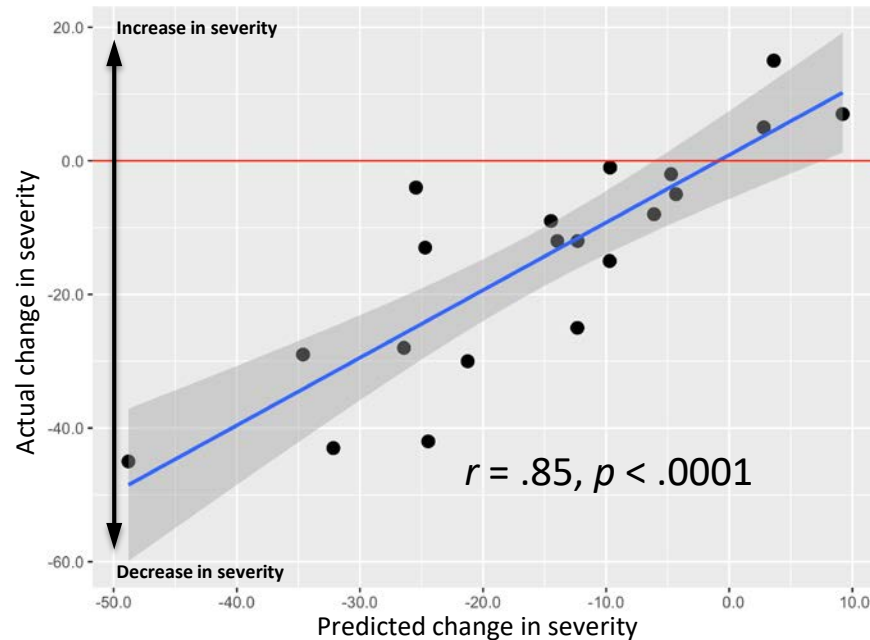
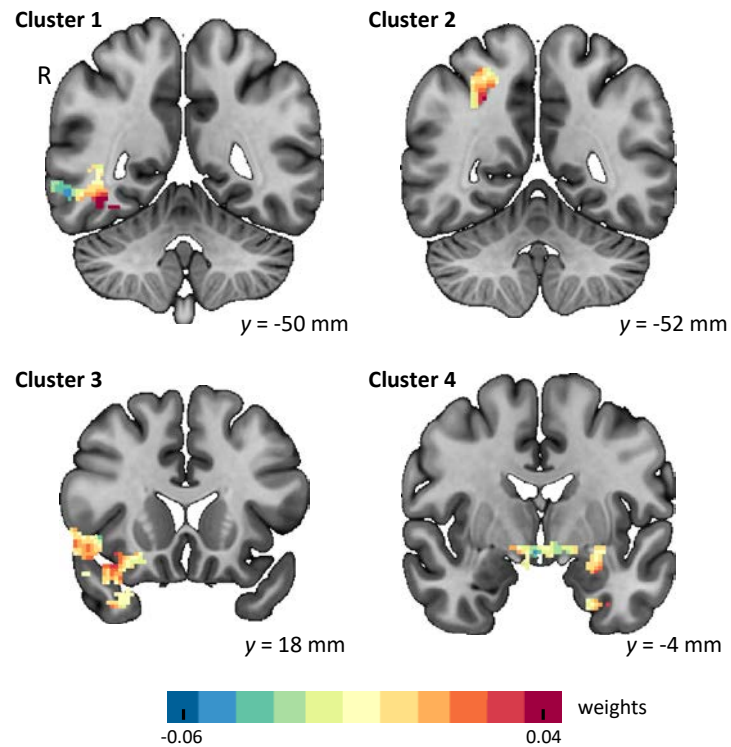
Pivotal Response Training (PRT)



Change in Behavior: Social Responsiveness Scale (SRS)



Neuro-prediction of treatment response



Yang et al. (2016)
Translational Psychiatry

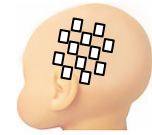
Linking genes, brain,
& behavior in the
longitudinal study of
infants social brain
development



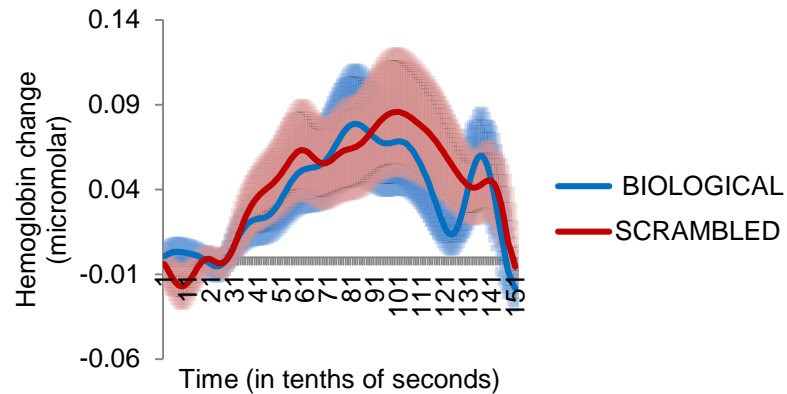


Results: fNIRS (LR and HR 3-Month-Old Infants)

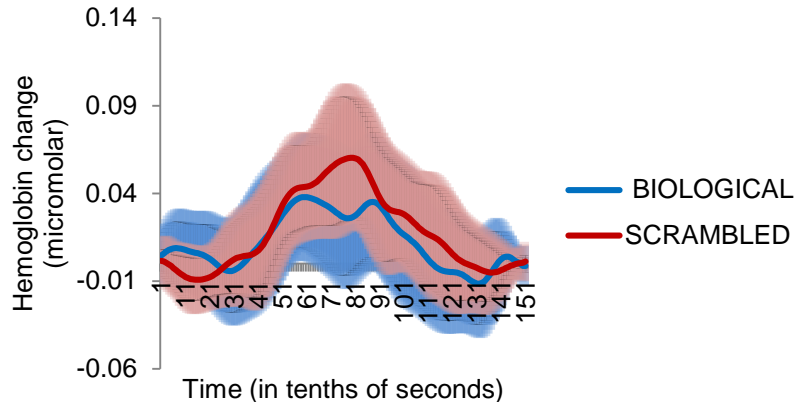
LEFT



Low Risk



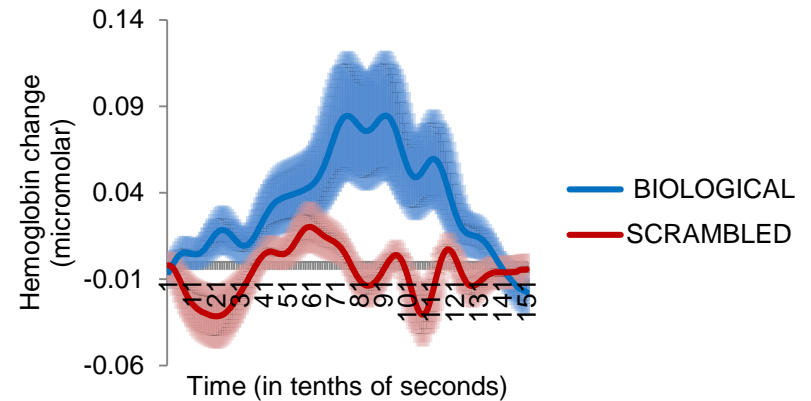
High Risk



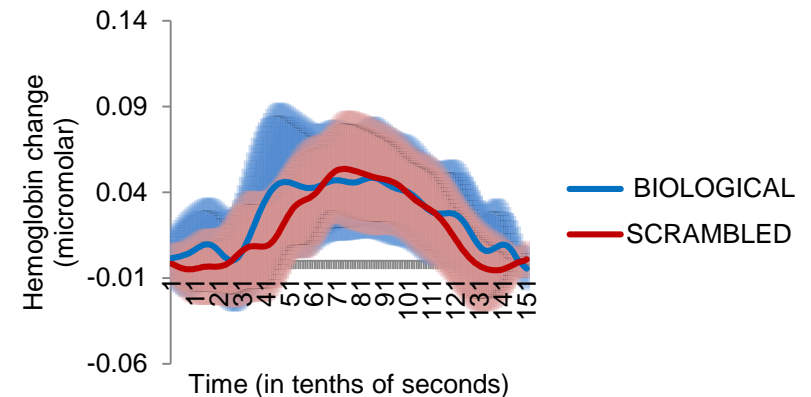
RIGHT



Low Risk



High Risk



Universal Screening?



Ashley Darcy-Mahoney, PhD,
NNP, FAAN

3,600 births per year
representing all ethnicities,
classes, backgrounds – a
population-based sample



Acknowledgments

NIMH

NICHHD

NINDS

The Carbonell Family

The Harris Family

The Dietz Family

Simons Foundation

Autism Speaks

Hilibrand Foundation

John Merck Scholars Fund

Autism Science Foundation

We thank the participants and their families for participating in our research.

We thank my colleagues who make this work so much fun.

kevinpelphrey@gwu.edu

Girls and Women with ASD— Clinical Perspectives

Pam Ventola, PhD
Assistant Professor

Yale Child
Study Center

SINCE 1911

childstudycenter.yale.edu



Yale SCHOOL OF MEDICINE



Learning Objectives

- **Identify clinical differences between females and males with ASD**
- **Describe factors related to misdiagnosis or delayed diagnosis in females with ASD**

Differential Prevalence

- Sex Ratio → 4:1; as high as 8:1 in individuals with IQ > 70
- Girls diagnosed later than boys
 - Mean age of 3 years for boys
 - Mean age of 4 years for girls

Boys and Girls Differ

- Girls and boys are different.
- Biological? Socially constructed?



Social Demands Differ



Differences in Social Expectations

- Boys (and men):
 - Large stable groups; rough and tumble play; competitive team games; socialize through activities
- Girls (and women):
 - Small groups; conversational; intimacy through sharing

The Classic Female Phenotype

- Often, girls with ASD compared to boys with ASD:
 - Lower cognitive abilities
 - More severe social communication deficits
 - Fewer externalizing behaviors
 - Fewer repetitive behaviors/restricted interests
- What about the more cognitively able girls?

Females and Males with IQ >70

- Boys with ASD
 - More isolative
 - Unusual interests (mayors, portable toilets, schedules)
 - Disruptive behaviors
- Girls with ASD
 - Strong interests but consistent with TD peers
 - Greater internalizing symptoms (anxiety, depression)

Case Vignette

- Diagnosed with ASD at 4 years old
 - Nonverbal skills ~ 2.5 year level; Language skills ~ 2 year level
 - “Talked” constantly
 - Flitted about, repetitively “dancing”
 - Hyper-focused on own reflection
 - Fixated on Disney princesses
 - Very directive and rigid

Case Vignette

- 10 year old girl with ASD
 - Nonverbal abilities: below average; verbal abilities: average
 - Highly socially motivated, outgoing, and talkative
 - No disruptive behaviors
 - “Hyper-feminine”
 - Focused on style, celebrities, boys
 - Fixated on peers
 - Learn about peers, follow peers, want to be close to peers (over-bearing to others)

Why are we missing or delaying diagnosis of ASD in girls?

Standardized Diagnostic Measures

- Biased towards typical ASD male presentation
 - Girls report problems with relationships but teachers report fewer symptoms
 - Clinical settings- boys are more active and outwardly atypical
 - Boys have more atypical interests and more repetitive behaviors
 - Easier to identify as RRBs

Girls with ASD Mask Difficulties?

- Elementary school-aged children (Dean et al., 2017)
 - Girls with ASD maintain physical proximity but not engagement
 - Girls are flitting in and out of social groups
 - Adults see girls with ASD together with other girls, but peers detect differences
 - Boys with ASD were more isolative
 - Boys have trouble initiating and sustaining
 - Adults see boys as being excluded/alone

Continuing to Mask Inherent Difficulties

- Adults with ASD also “camouflage” symptoms
 - Use learned jokes, follow social scripts, mimic others’ gestures/facial expressions
 - Adopt persona from peer or fictional character
- Women use these camouflaging strategies more readily and often (Lai et al., 2017)
- Camouflaging may bring increased stress and anxiety; “exhausting to be someone you are not”

Delayed or Misdiagnosis in Females

- Differing gender-based expectations
- Differing presentations
- Function of bias in diagnostic instruments
- Compensatory strategies (masking/camouflaging)

Treatment and Support for Girls with ASD

Behavioral Interventions

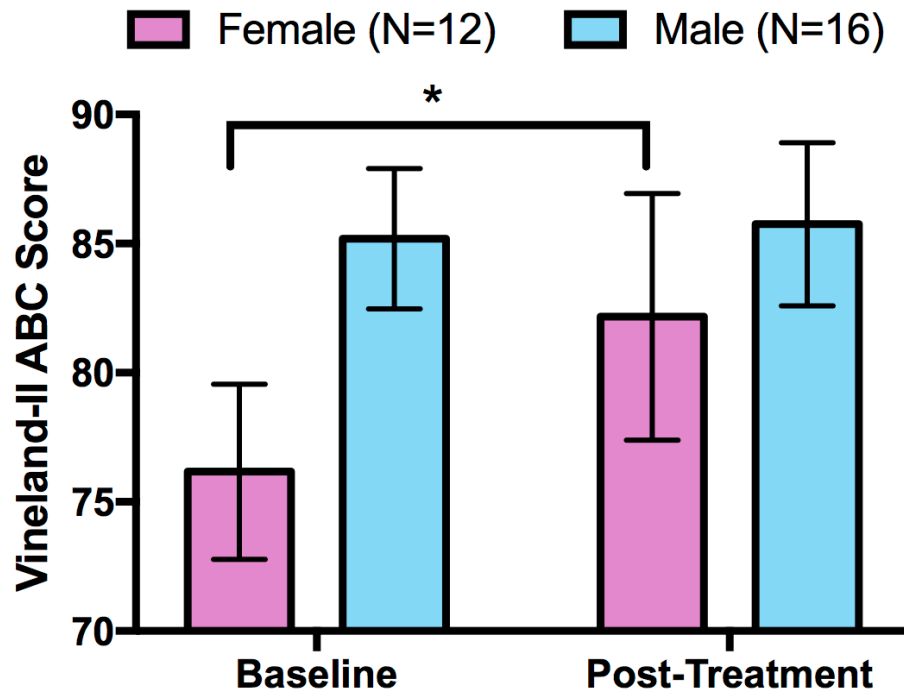
- Multiple evidence-based naturalistic behavioral interventions
- Pivotal Response Treatment (PRT)
 - Combines applied behavior analysis principles with motivational strategies
 - Focuses on pivotal areas with widespread change in functioning

Supporting Girls with ASD

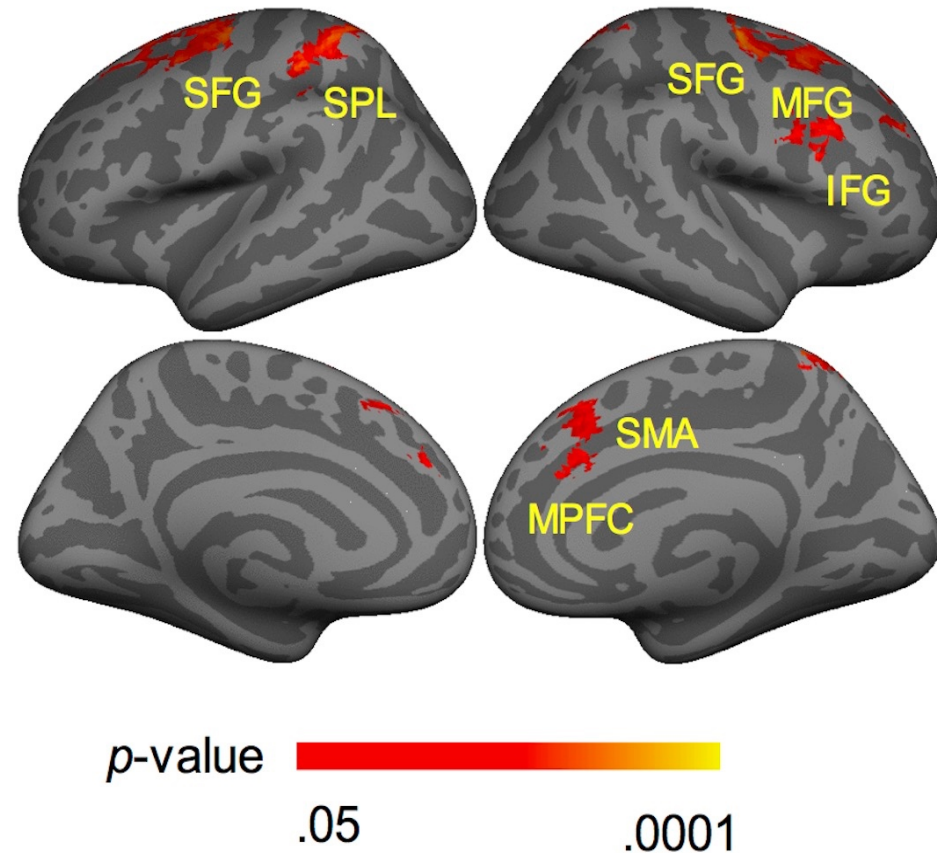
- 28 children; 16 boys/12 girls (4-7 years) received PRT
- 4-month treatment course
 - 8 hours per week
 - Direct work with child & parent in clinic & home

<i>Variable</i>	<i>M</i>	<i>SD</i>
Age	5.48	0.85
DAS-II	102.8	16.7
CELF-4 Core Language	103.5	13.7

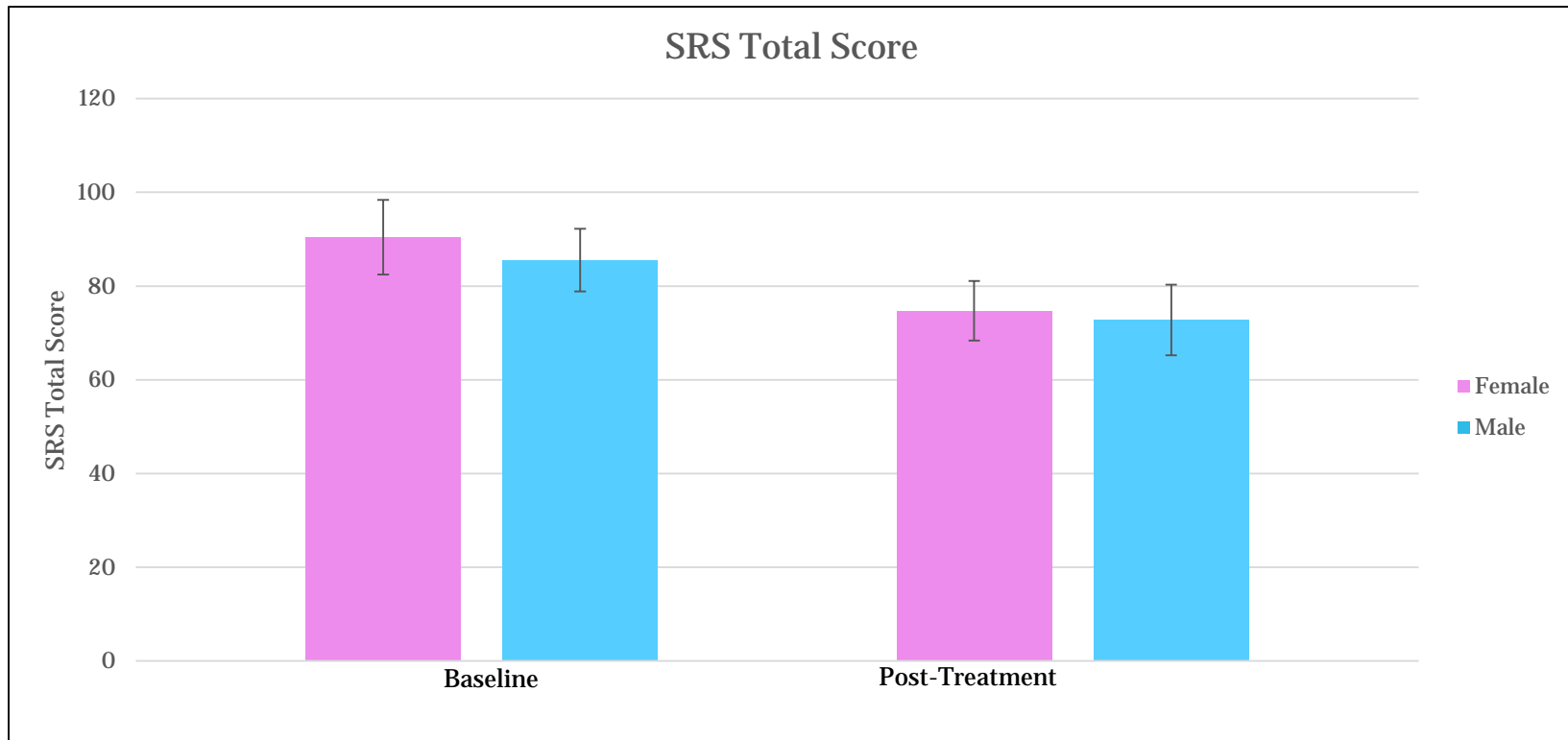
Supporting Girls with ASD



(B) Neural prediction, slope: ♀ > ♂



Supporting Girls with ASD



- Overall improvement in social communication skills
- No sex-based differential in improvement

Acknowledgements

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- NIMH
- NIH
- Simons Foundation
- Deitz Family
- Esme Usdan and Family
- Schmid Family
- Dwek Family
- Women's Health Research at Yale
- Autism Science Foundation

Dr. Pam Ventola

pamela.ventola@yale.edu



ASAN

AUTISTIC SELF ADVOCACY NETWORK

Autistic Women and Girls & Research

- More autistic people exist than have been diagnosed
 - Underdiagnosis widens this gap for women and people of color
- Diagnostic disparities → research → diagnostic disparities → research....

Autistic Women and Girls & Diagnosis

- Common experiences of being diagnosed
- Consequences of not having a diagnosis
- Consequences of getting diagnosed

Autistic Women and Girls & Myths About Autism

- Empathy
- “Extreme maleness”

Autistic Women and Girls

Struggles

- Health care
- Autistic women and girls face violence and abuse
- Employment
- Access to community-based services

Autistic Women and Girls

Strengths

- Autistic people & strengths (generally)
- Resilience
- We want a better future for autistic children & adults

What is the best way to address the needs of autistic girls & women?

- Ask us

Autistic Self Advocacy Network: autisticadvocacy.org

Autism Women's Network: autismwomensnetwork.org

Academic Autism Spectrum Partnership in Research and Education: aaspire.org