

# Building Precision Care for Autism(s)

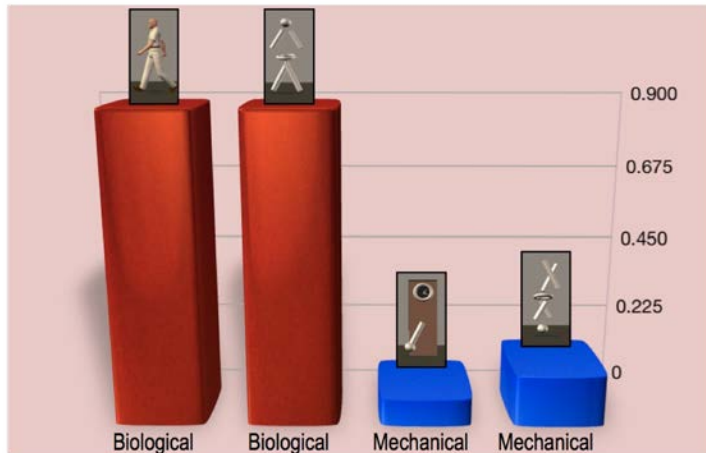
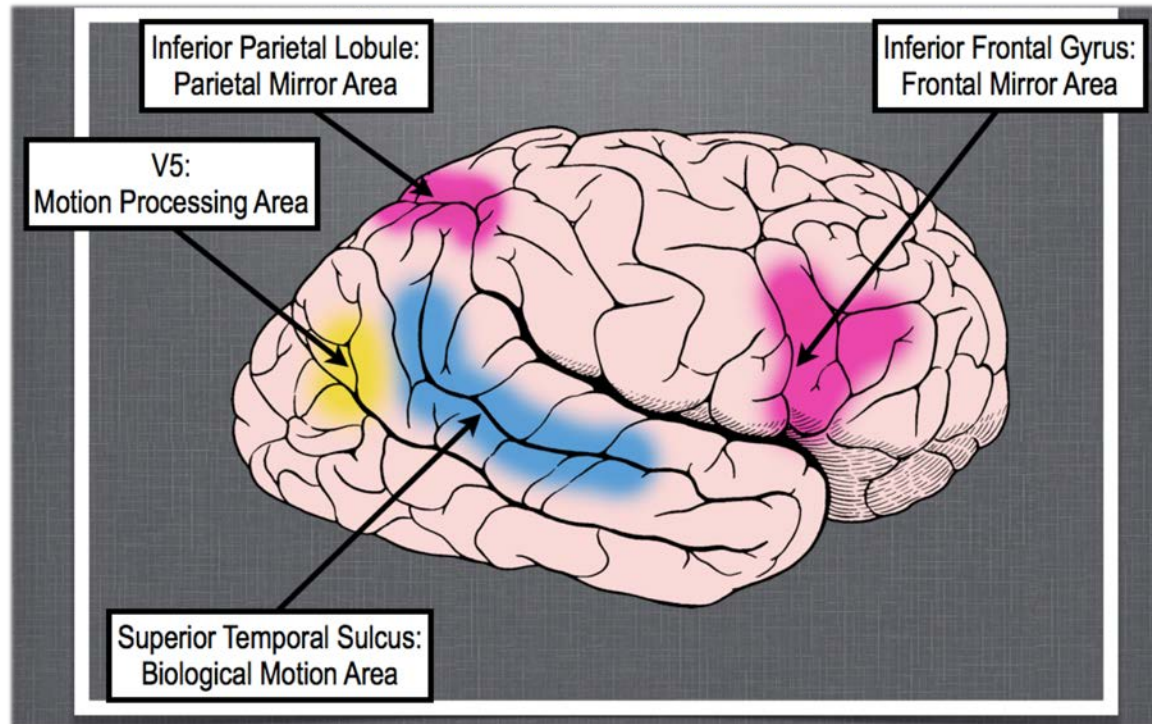
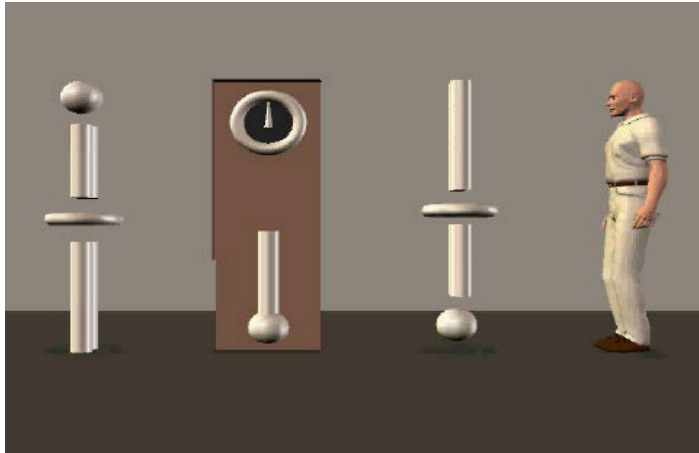
*Kevin Pelphrey, PhD*

*Harrison-Wood Jefferson Scholars Foundation Professor of Neurology*



**Problem:** Lack of mechanistically informed *biological markers* perpetuates the *status quo* of inexact treatments, wasted time and resources, failures to optimize progress for children and families.

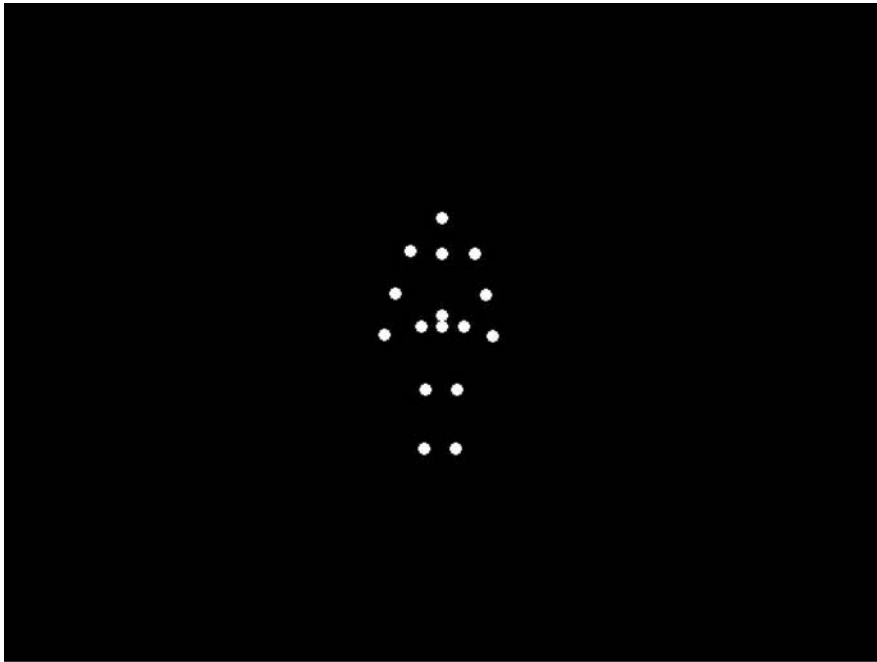
# The Social Brain



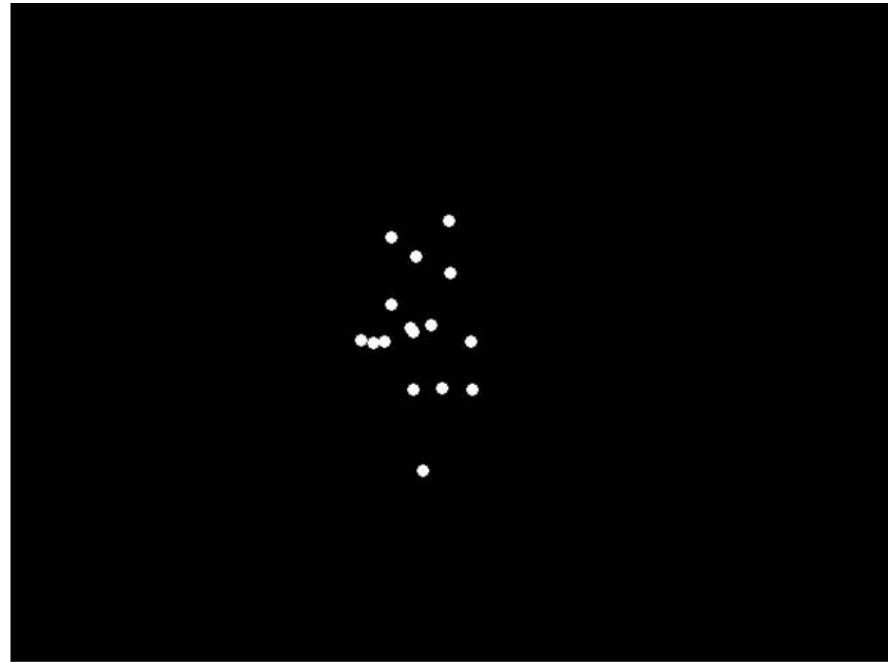
Pelphrey et al. (2003) *Journal of Neuroscience*

# Social vs. Non-Social Motion

Coherent  
Biological (BIO)

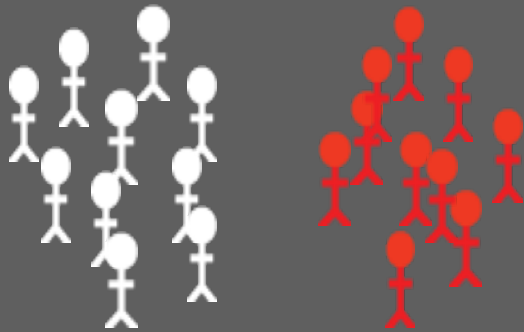


Scrambled  
Biological (SCRAM)



Sensitive, reliable brain measures that are informative at the level of the individual

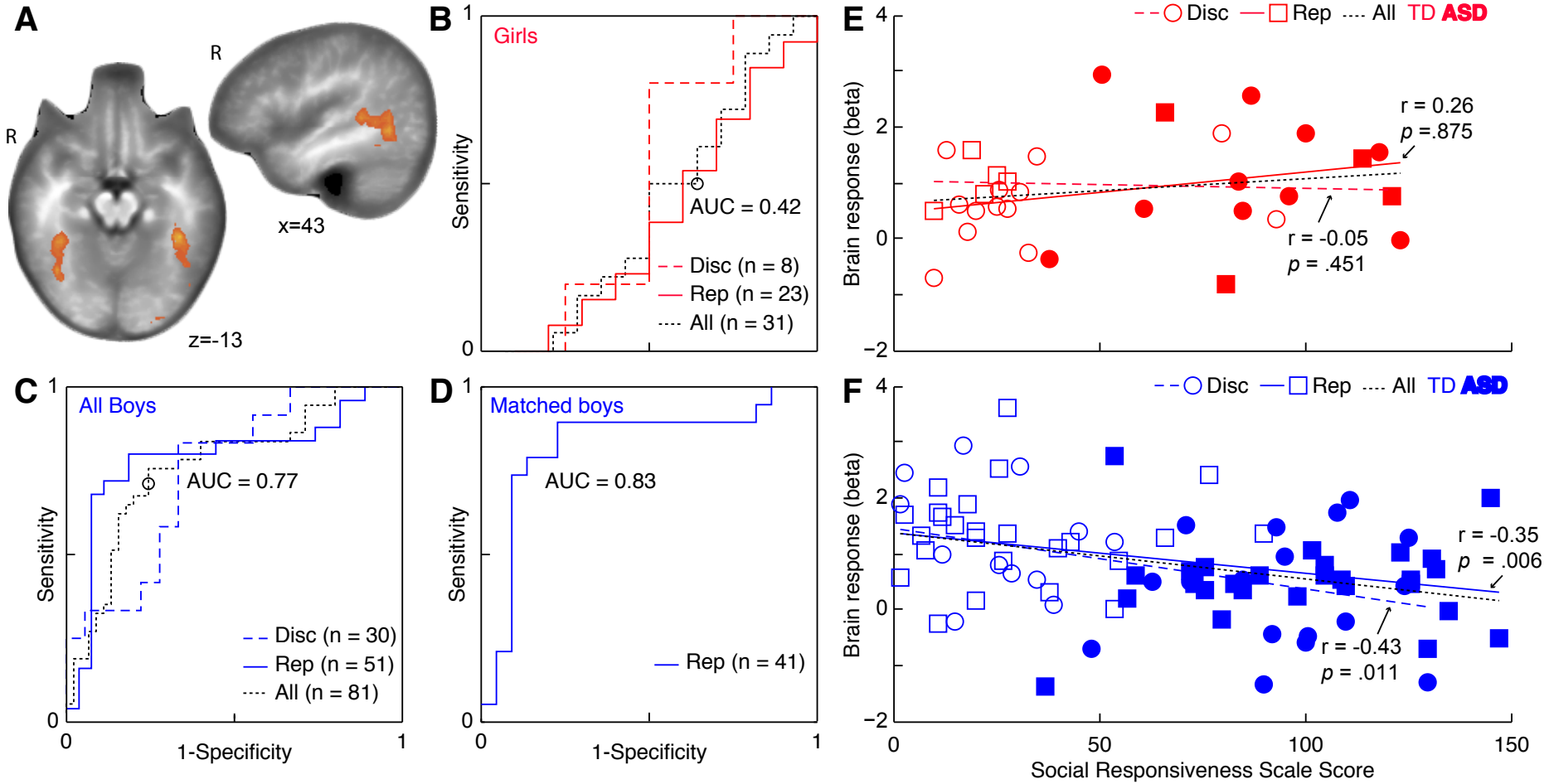
*Discovery*



*Replication*

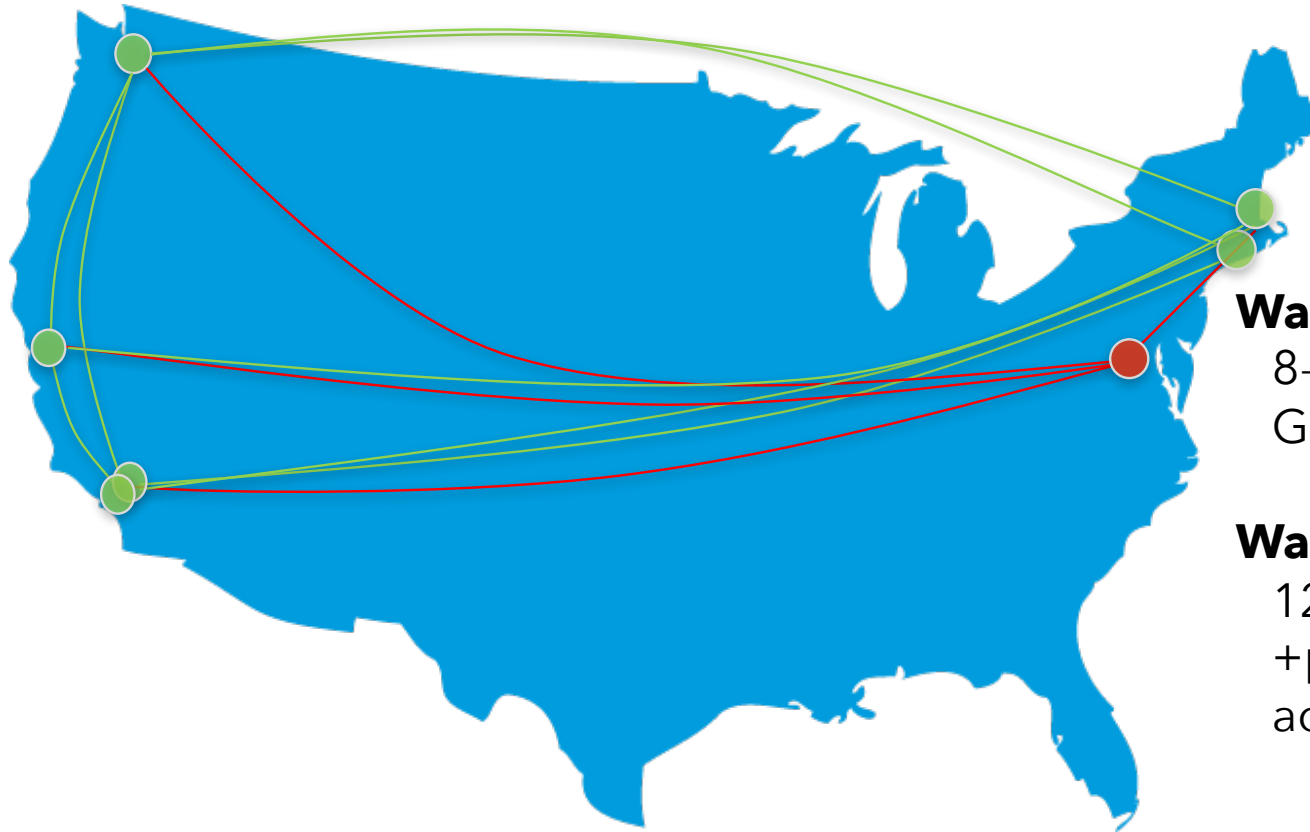


Björnsdotter et al. (2016) *JAMA*



Björnsdotter et al. (2016) *JAMA*

# NIH Autism Center of Excellence (ACE): Girls' Neurogenetics Network



**Wave 1** (2013-2017):  
8-17y;  $Ns = 250$   
Genes, brain, behavior

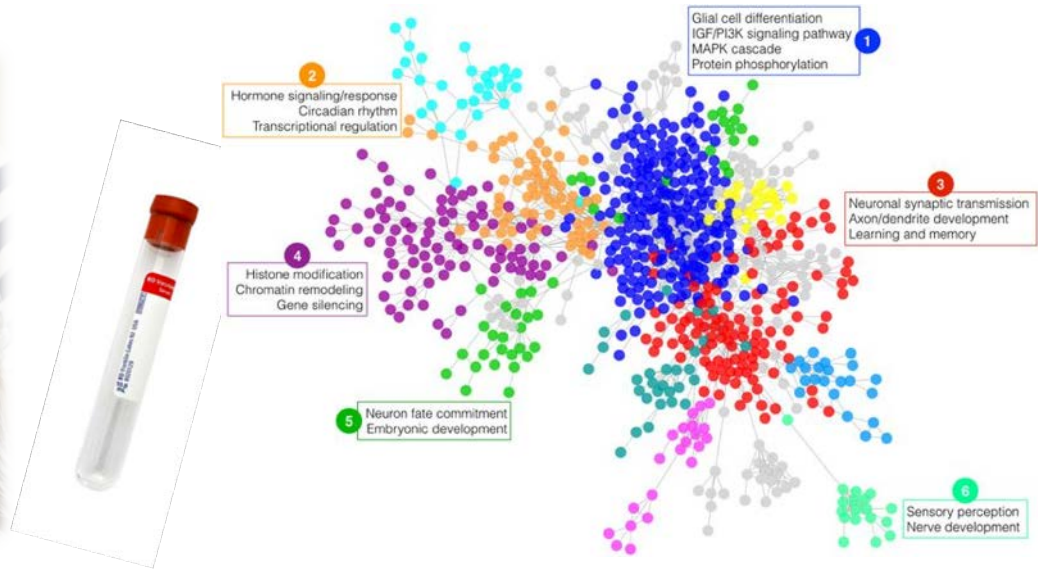
**Wave 2** (2019-2022):  
12-26y;  $Ns = 250$   
+personal experience &  
adult outcomes

THE GEORGE  
WASHINGTON  
UNIVERSITY  
WASHINGTON, DC

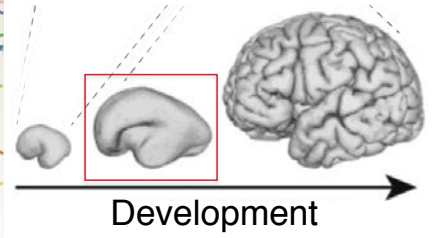
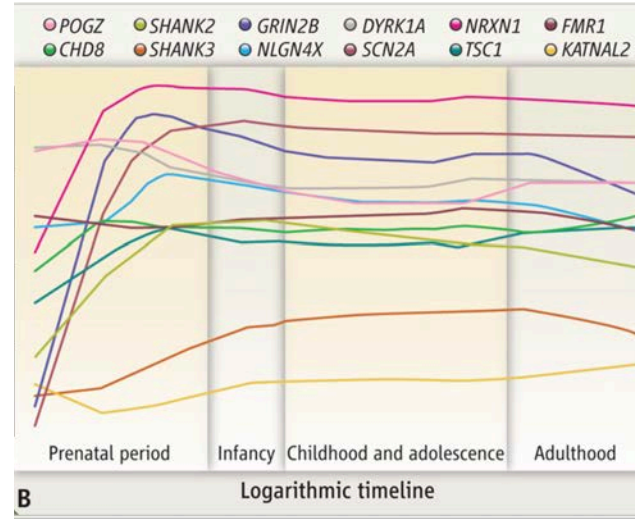


UNIVERSITY  
of VIRGINIA

# NIH ACE Neurogenetics Network



Duda et al. (2018) *Translational Psychiatry*

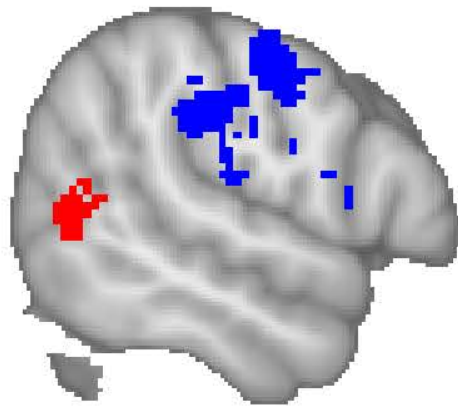


Development

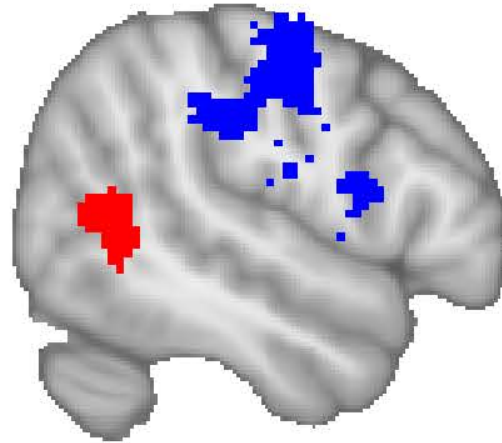
*What genes regulate these ASD risk networks?*



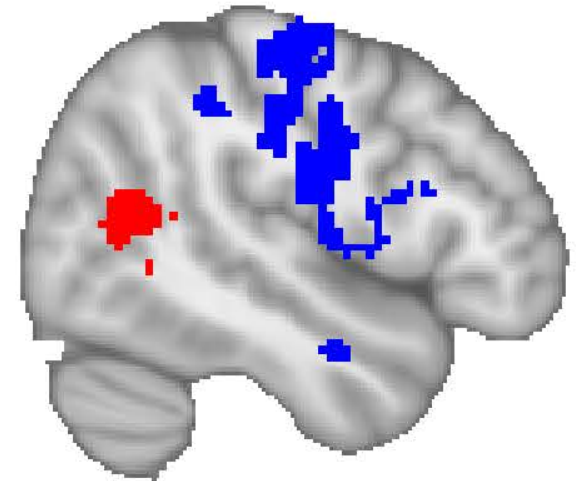
ASD♀ neural signature does not overlap with ASD♂ neural signature



x = 56



x = 52



x = 48

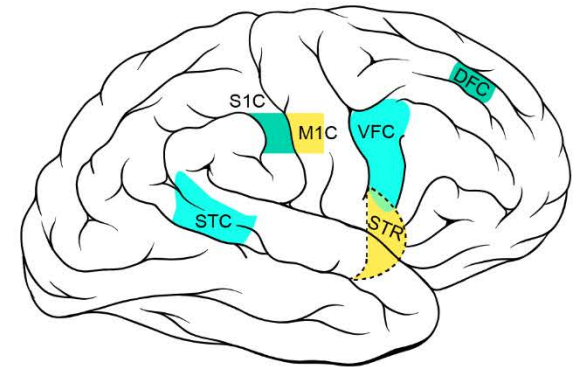
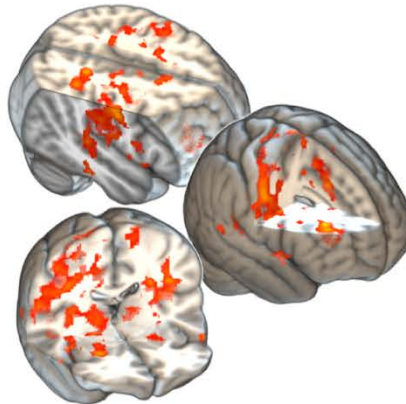
- TD♀-ASD♀ cluster-wise  $z < 2.3, p < .05$
- TD♂-ASD♂ cluster-wise  $z < 2.3, p < .05$

# Creation of Criteria Gene-Set

Regions characterized in BrainSpan  
Developmental Transcriptome (Periods 3-10)

ASD♀ Neural Signature regions (TD♀ > ASD  
♀ response to BIO-SCRAM)

Criteria gene-set: ASD♀ Neural Signature Regions  
Genes with any positive expression in these sites periods 3-10



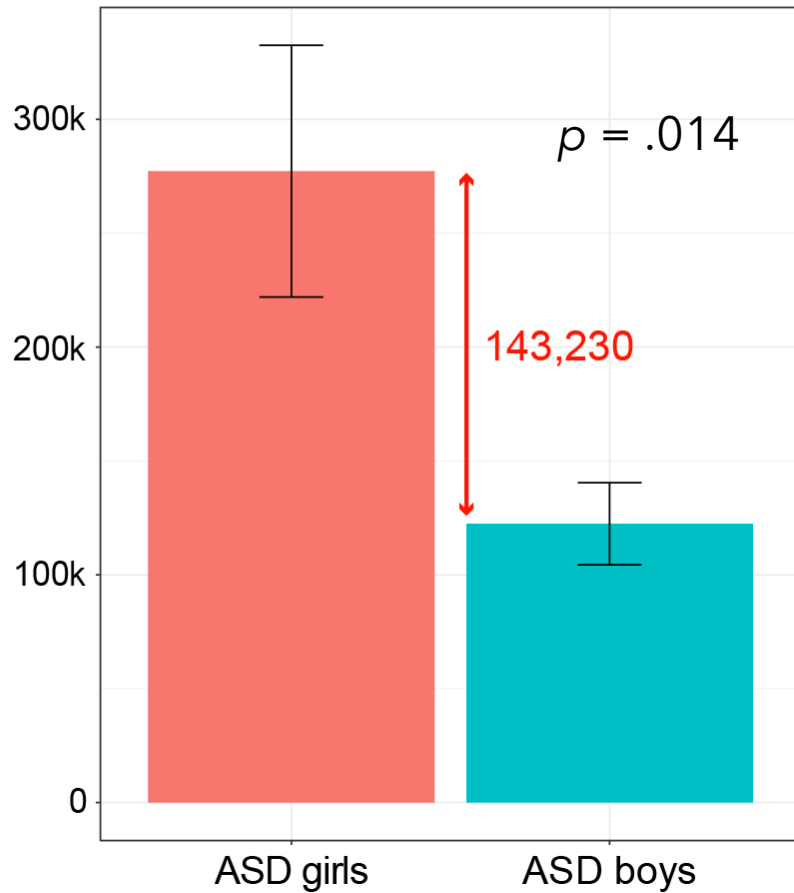
M1C: Primary motor cortex, R & L    DFC: Dorsolateral prefrontal cortex, R & L  
STC: Superior temporal cortex, R    S1C: Primary somatosensory cortex, R & L  
STR: Striatum, R & L    VFC: Ventrolateral prefrontal cortex, R & L

“Spatio-temporal  
transcriptome of the  
human brain”

Kang et al., 2011, *Nature*

Jack et al. (in press) *BRAIN*

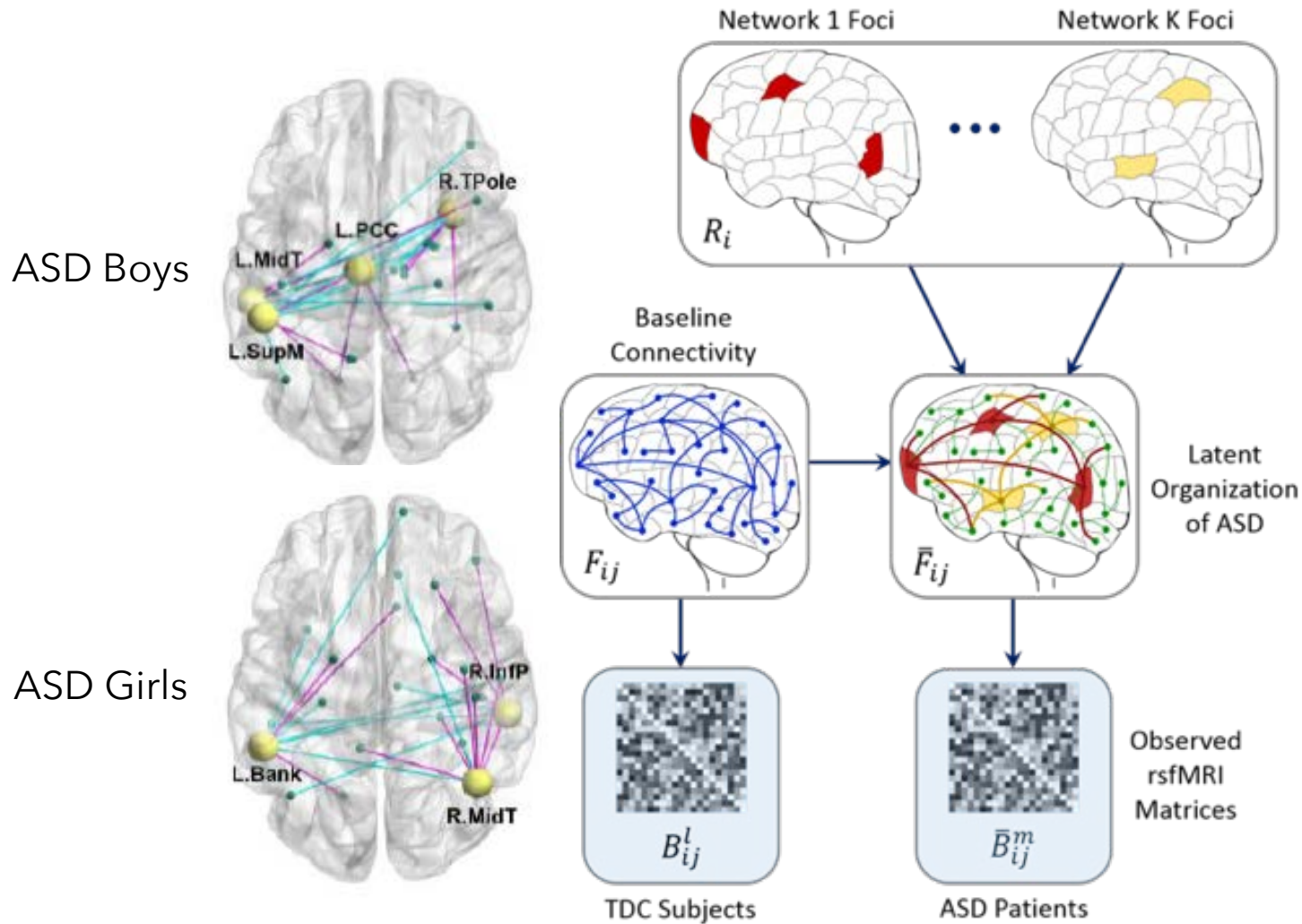
## All ASD♀ Neural Signature Regions



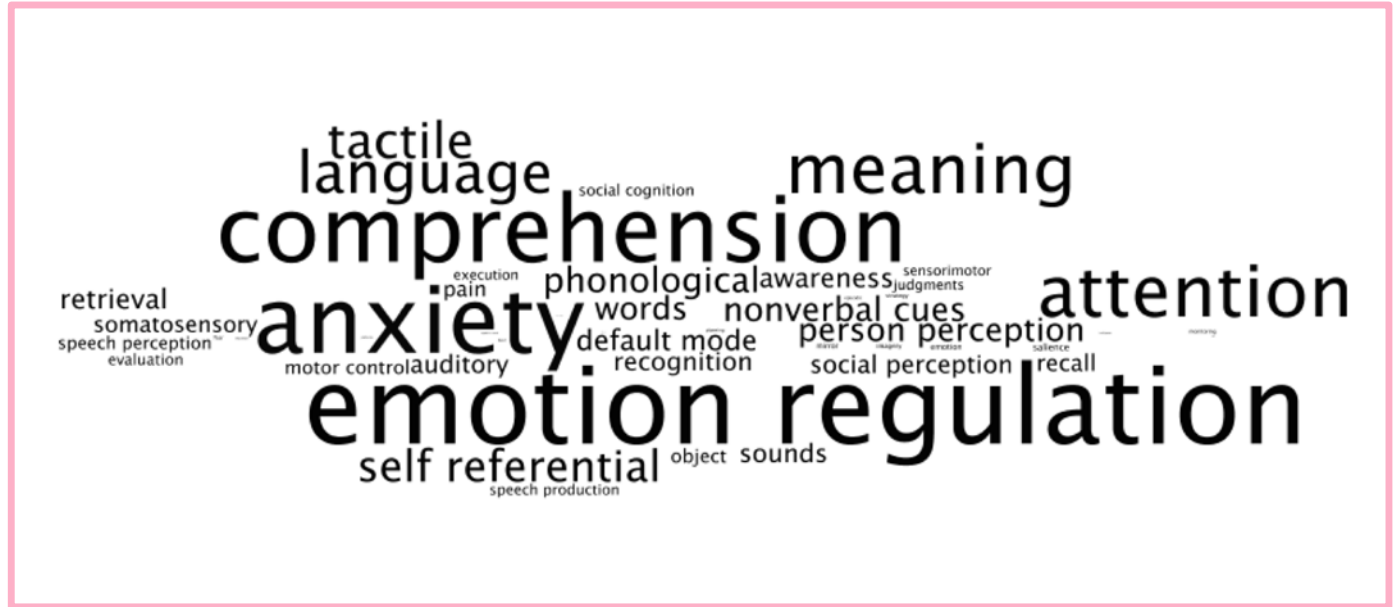
Versus♀-♂ mean difference  
&  $p$ -value in:

Randomization Test	$p$	
All CNVs	.0005	} $n$ CNVs held constant
All CNVs, sex-specific	.0011	
Exon array	.0000	
Exon array, sex-specific	.0434	
Within criteria set, randomize sex	.0037	
Select 11 random Brainspan regions ( <i>can include original regions</i> )	.1903	

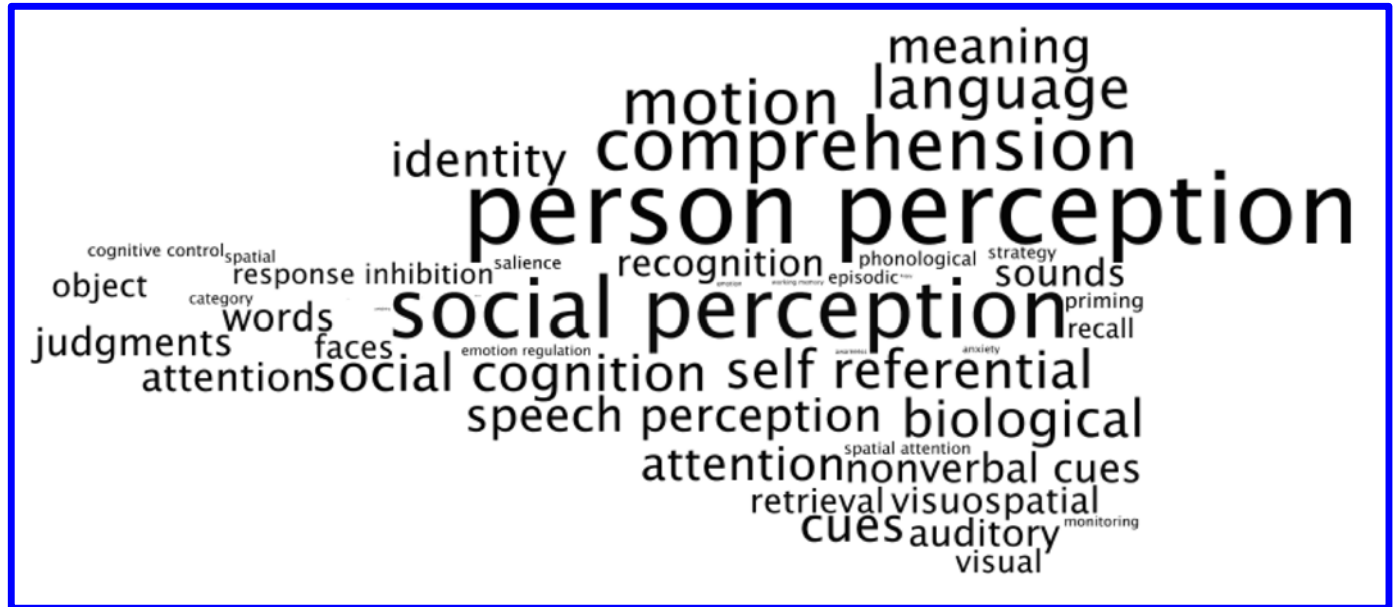
# Brain networks "speak to us"



Girls -  
Network to  
Construct  
mapping

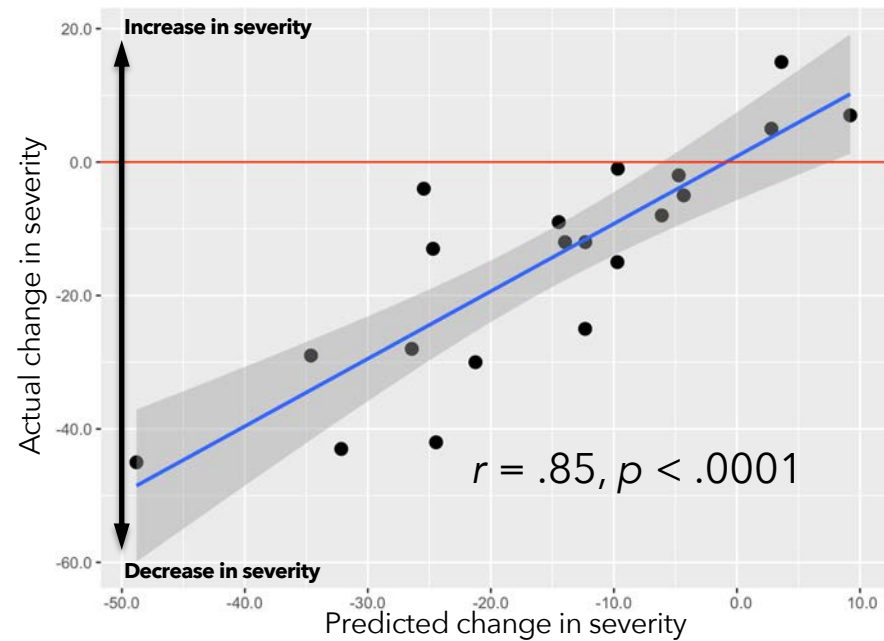
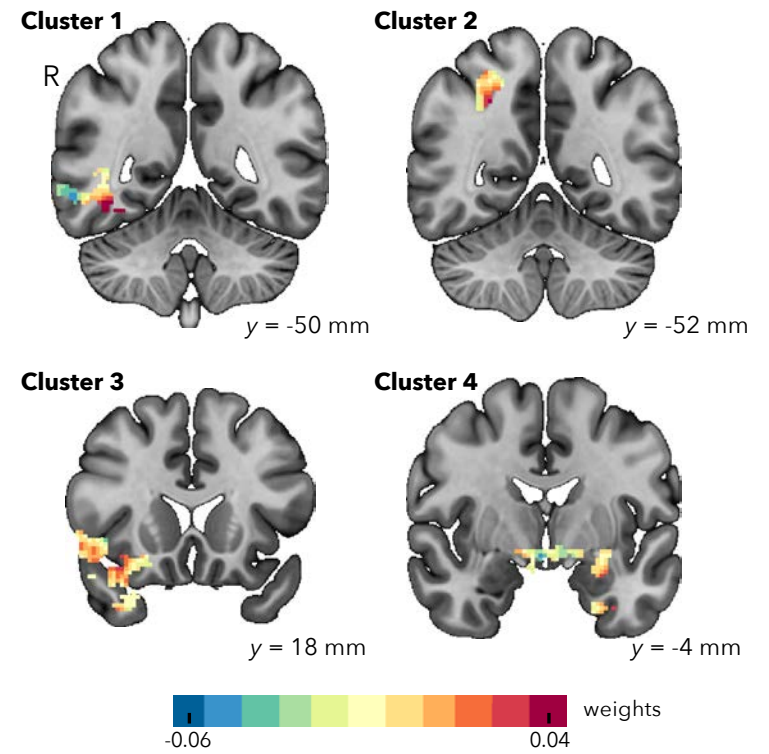
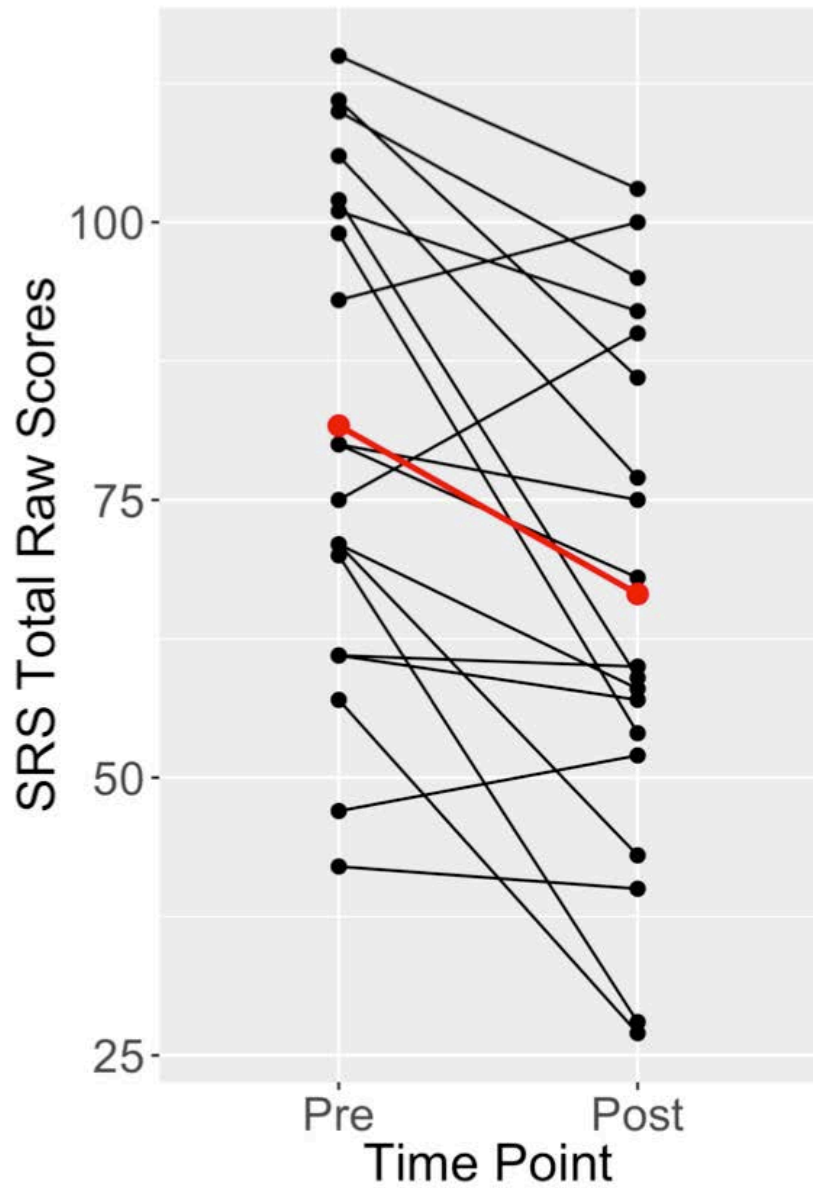


Boys -  
Network to  
Construct  
mapping

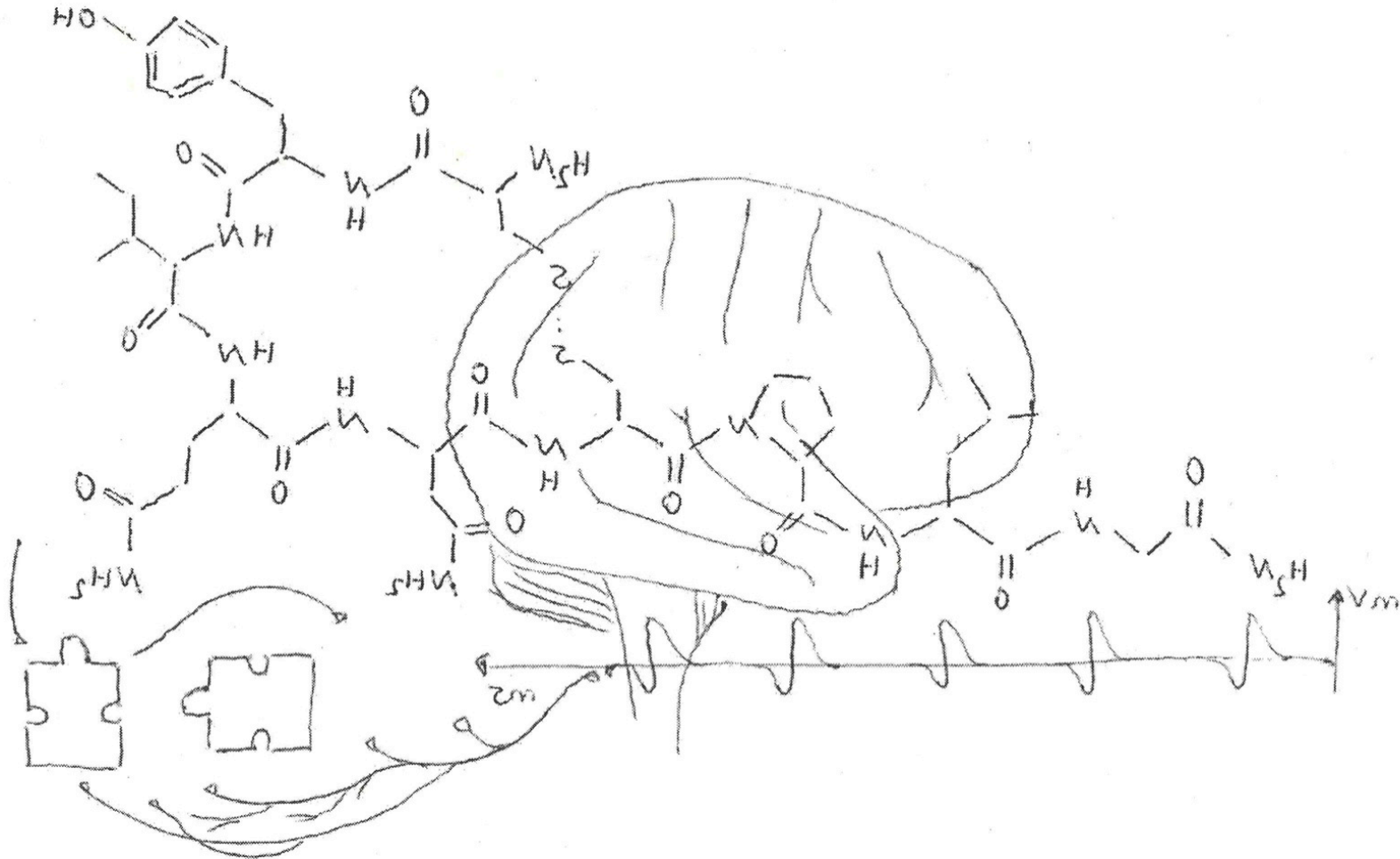


# Predicting treatment response & revealing mechanisms of change



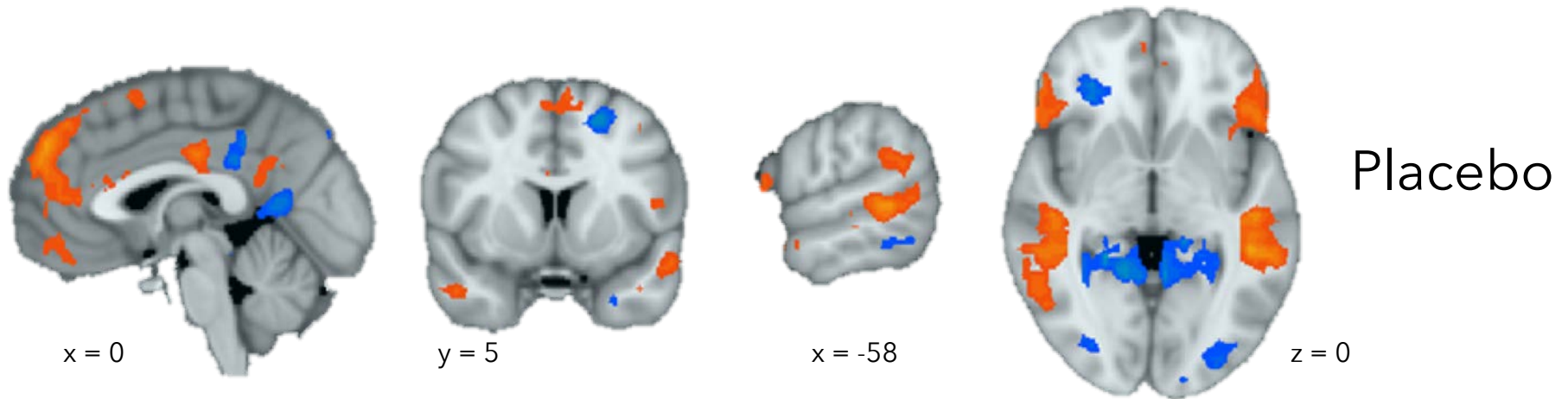
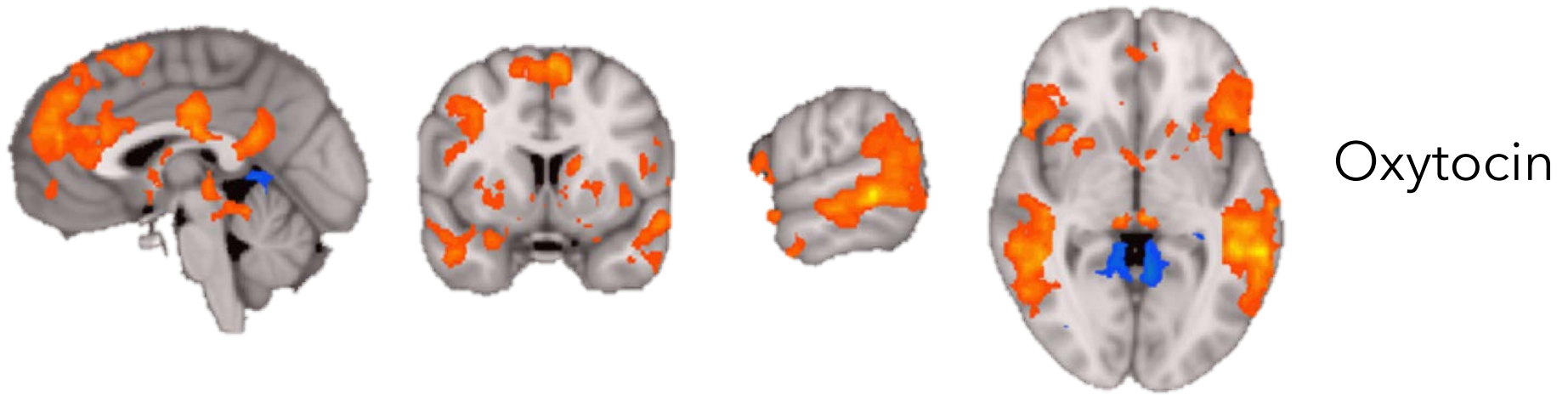


# Levers to improve behavioral treatment response





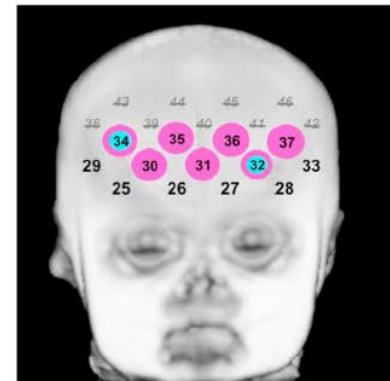
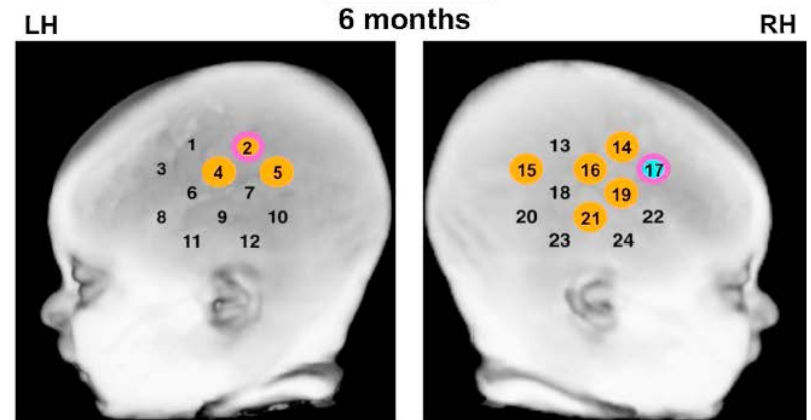
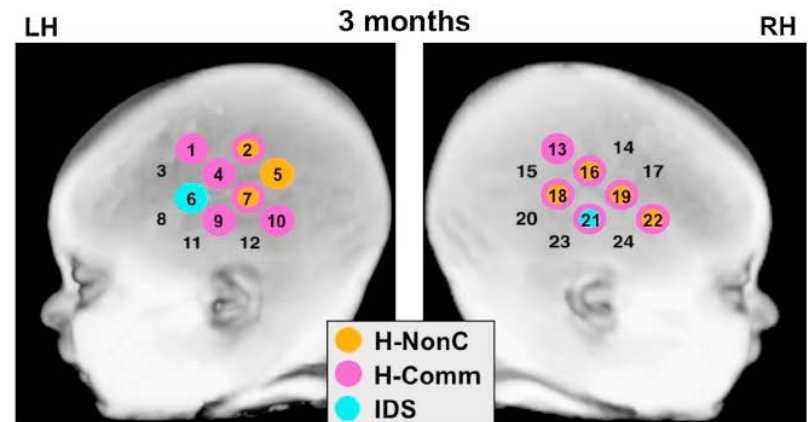
# Intranasal Oxytocin



Gordon et al. (2013) *PNAS*



# fNIRS: Predicting language development from early brain response to infant directed speech



\* Increase in HbO depicted in lateral arrays and decrease in frontal array

# Newborn screening for social development



In a Population-  
representative  
sample

# Acknowledgments

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Wood Family	
Dietz Family	

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