



# Heart-Defined Sustained Attention in Infant Siblings of Children with Autism

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# INTRODUCTION

# “High Risk” Infants

- Autism spectrum disorder (ASD) affects 1:42 U.S. males
  - Impaired social communication, repetitive behaviors
  - No biomarker
- Predicting ASD in infants → early detection, prevention
- Infant siblings of children with ASD (ASIBs) = 19% risk
  - Over 100 ASIB studies in last decade
- ASIBs at risk for multiple outcomes
  - Warrants mechanism-specific research



# “High Risk” Infants

Two complementary approaches to “high risk” studies:

- 1. Examine prodromal features of ASD**

- Outcome: identify predictors of later diagnoses

# “High Risk” Infants

Two complementary approaches to “high risk” studies:

## 1. Examine prodromal features of ASD

- Outcome: identify predictors of later diagnoses

## 2. Examine endophenotypes

**Endophenotype:** a measurable, heritable trait that associated with a clinical profile  
(Gottesman & Gould, 2003)

- Characterize broader phenotype
- Outcome: characterize genetic associations, risk

# “High Risk” Infants

**Broader Autism Phenotype:** subthreshold autism-associated features in first-degree relatives of individuals with autism (Baron-Cohen, 2004; Folstein & Rutter, 1977)

## Discrete Trait

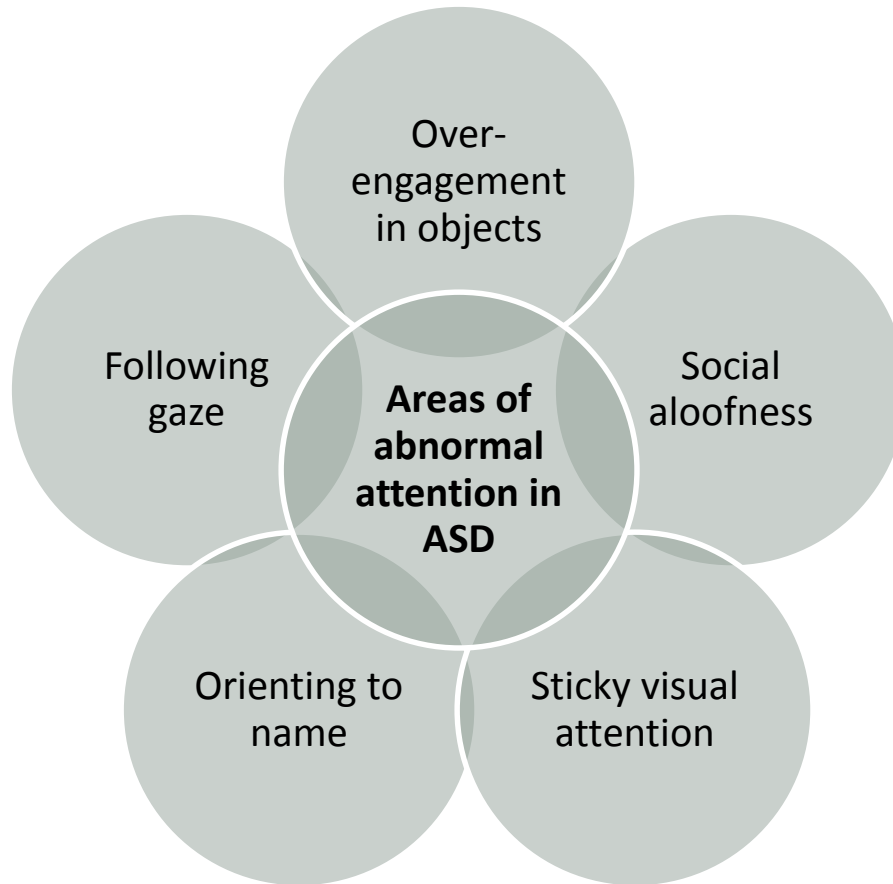


## Continuum



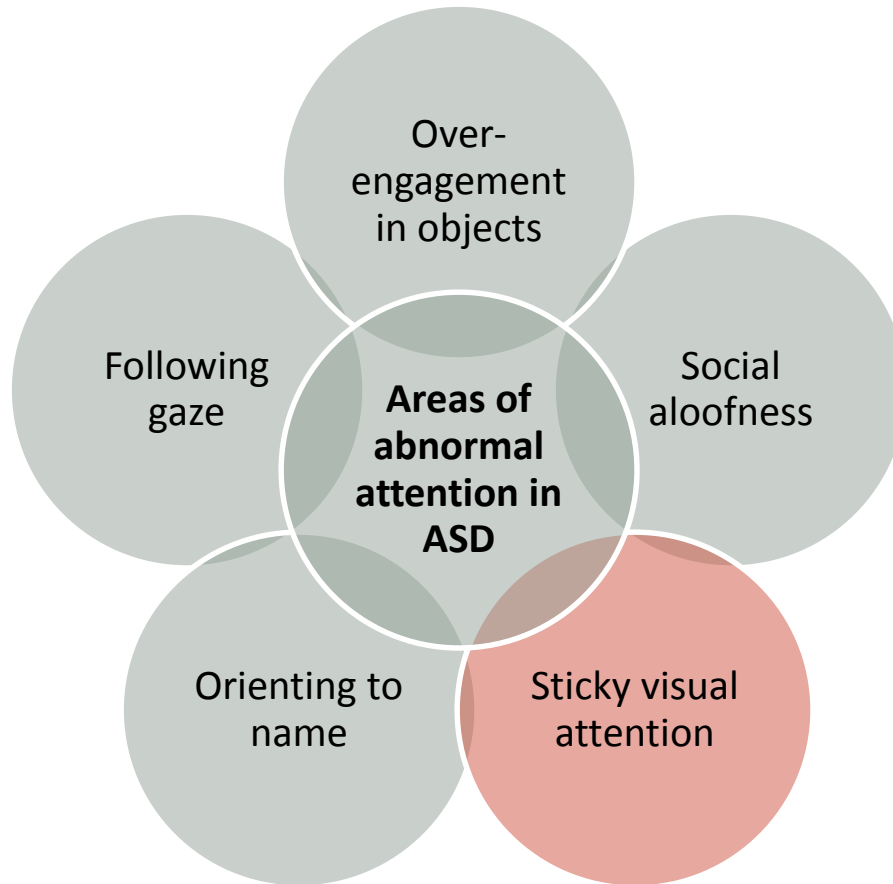
# Attention in ASD

Is abnormal attention an **endophenotype** of ASD?



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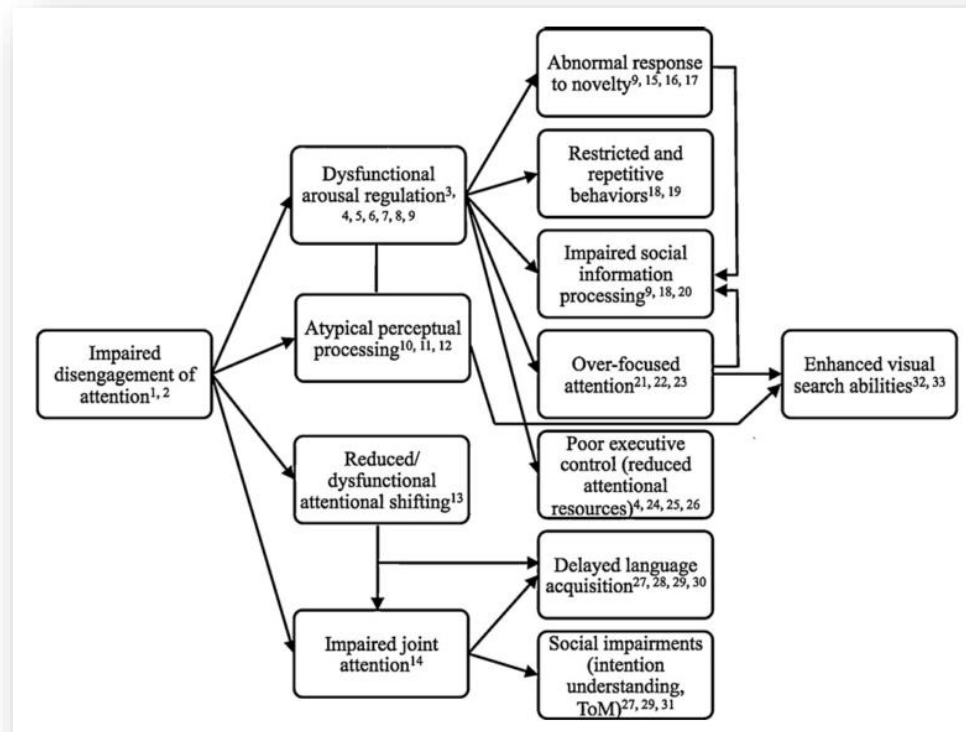
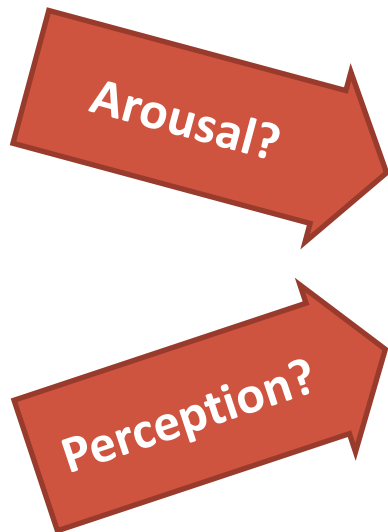


# Orienting and Disengagement

- Infants at risk for ASD show impaired disengagement from 6-12 months of age (Elsabbagh et al., 2009, 2013; Zwaigenbaum et al., 2005; Elison et al., 2013)

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# Arousal

- Abnormal polyvagal functioning implicated in ASD (Bal et al., 2010; Klusek et al., 2015; Quintana et al., 2012)

**Polyvagal Theory:** Human autonomic system has evolved to maintain behavioral and psychosocial characteristics (Porges, 1995)

- Parasympathetic activity = regulated by vagus
- Vagus also controls
  - Facial muscles
  - Visceral processes (e.g. metabolic function, digestion)
- Abnormal arousal, facial expression, visceral processes in ASD

# Arousal

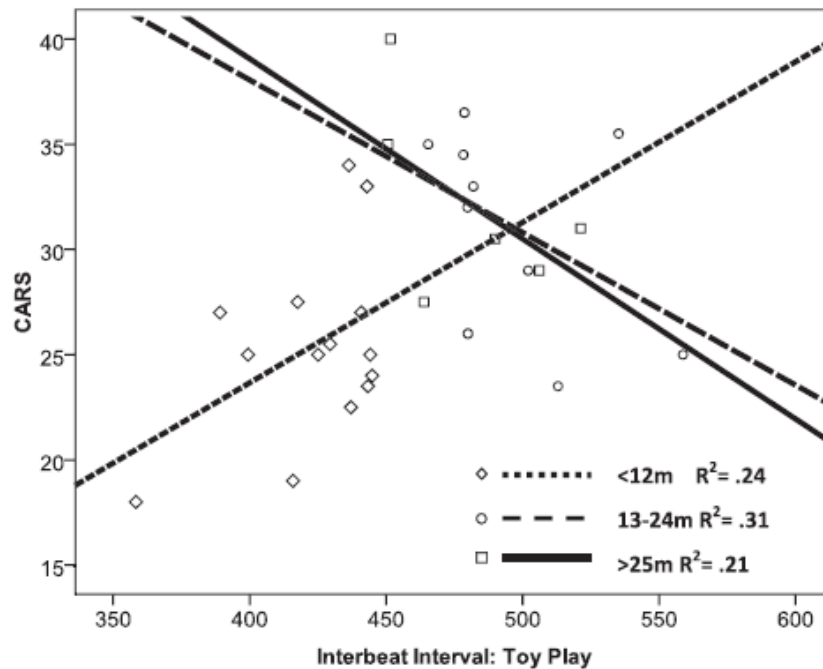


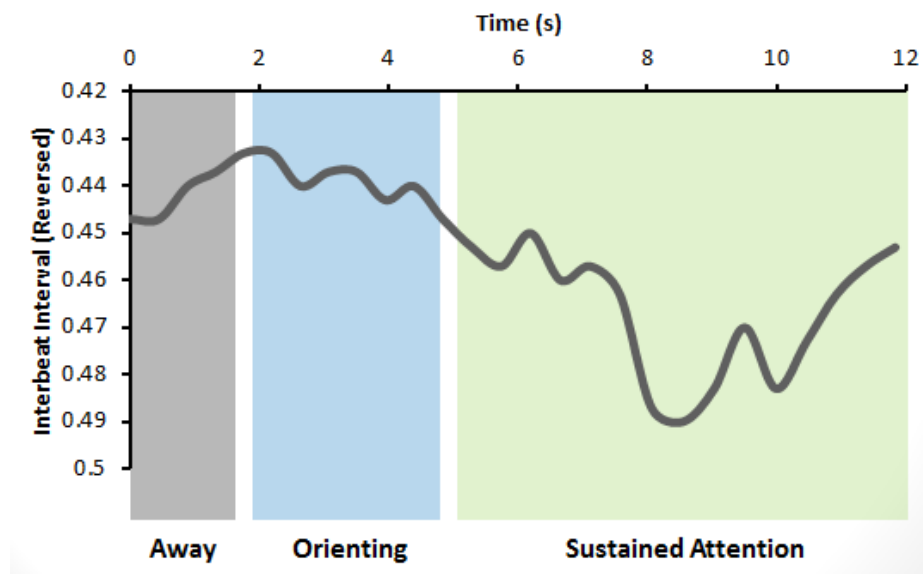
Figure 2. Cross-sectional interaction between age and interbeat interval (IBI) during toy play in the group with fragile X syndrome. CARS = Childhood Autism Rating Scale (Schopler, Reichler, & Renner, 1988). At younger ages, IBI was positively related with CARS outcomes. At older ages, IBI was negatively related with CARS outcomes. m = months.



Roberts, J.E., Tonnsen, B.L., Robinson, A., & Shinkareva, S.V. (2012). Heart activity and autistic behavior in infants and toddlers with fragile X syndrome. *American Journal of Intellectual and Developmental Disabilities*, 117, 90-102.

# Heart-Defined Attention

- Visual orienting and physiological arousal intersect (e.g. Casey & Richards, 1991; Richards, 2000)



- Infants in sustained attention are less distractible during:
  - computerized tasks (Casey & Richards, 1988; Richards, 1997)
  - behavioral tasks (Lansink & Richards, 1997; Roberts et al., 2011)

Could sustained attention inform orienting deficits in ASD?

# Questions & Hypotheses

## **BIOBHAVIORAL ASSOCIATIONS**

Greater sustained attention will be associated with greater behavioral looking

## **CROSS-GROUP DIFFERENCES**

ASIBs will display “extreme” behavioral and heart-defined sustained attention compared to controls

## **CLINICAL SIGNIFICANCE**

Abnormal behavioral and heart-defined attention will predict clinical autism risk at 11-14 months

# METHODS

# Participants

- 43 participants
  - 21 infant siblings (ASIBs)
  - 22 low risk (LR) controls
- Attention assessed between 1-3 occasions ( $n=77$  total)
- Attention data at all assessments; clinical data at 11-14 months
- Missing data: 22.2% ( $n=11$  per group)
  - 30% looking required for SA calculations (excluded 6 ASIB, 3 LR)
  - Physiological data excluded if >5% artifact



# Behavioral Measures

## Behavioral Looking

- *Baby Einstein* video (135s)
  - Inter-rater reliability = 83%
  - Coded using Noldus Observer



## Clinical Autism Risk

- *Autism Observation Scale for Infants* Total Score
  - Research reliability
  - Inter-rater reliability = 89%

## Mental Age

- *Mullen Scales of Early Learning* Early Learning Composite

# Heart Activity

**Collection**  
Alive System

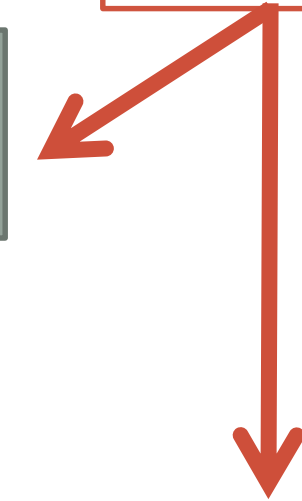
**Conversion**  
ATS Convert

**Editing**  
CardioEdit

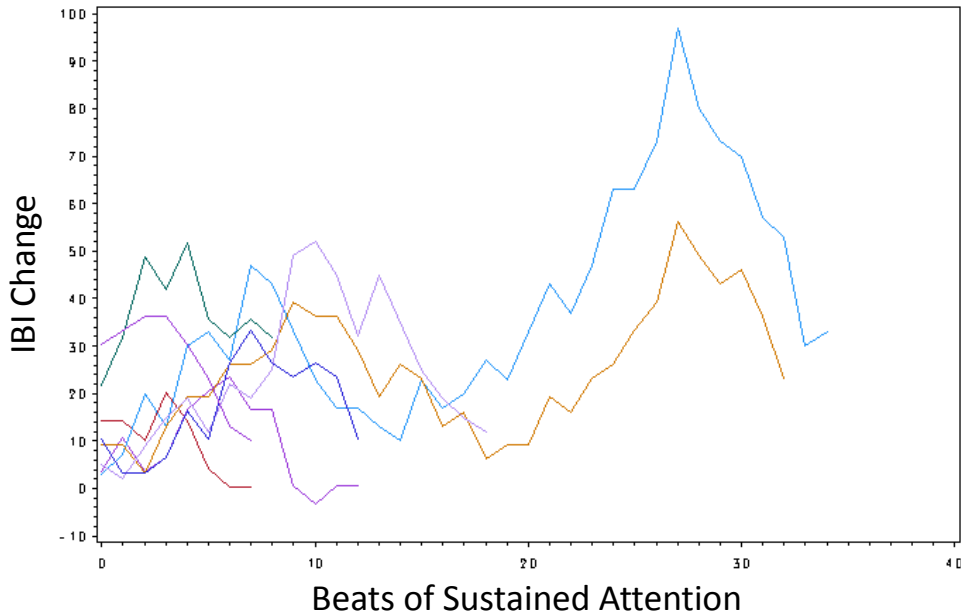
**Global Heart Activity**  
CardioBatch  
*IBI, RSA, IBI SD*

If > 5% Error  
Use behavior only

If  $\leq$  5% Error



**Heart Defined SA**  
Richards' SAS Algorithms  
*%SA, IBI Change, IBI SD*



# Analyses: MLM

	<b>Attention Related</b>	<b>Not Attention Related</b>
<b>Physiological</b>	Sustained Attention	Global Heart Activity
<b>Not Physiological</b>	Behavioral Attention	

# Analyses: MLM

**Level 1** (Unconditional Models): Examine DVs across age

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- Across our sample, what are DVs at the mean age of our sample, and how do these levels change over time?

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**Level 2** (Conditional Models): Effects of “predictors” on trajectories

- Group
- Clinical autism risk

# Results

- Proportion of time in behavioral and heart-defined attention correlated ( $\rho = -.69, p < .001$ )
- Proportion of time in behavioral attention not associated with global heart activity or features of SA

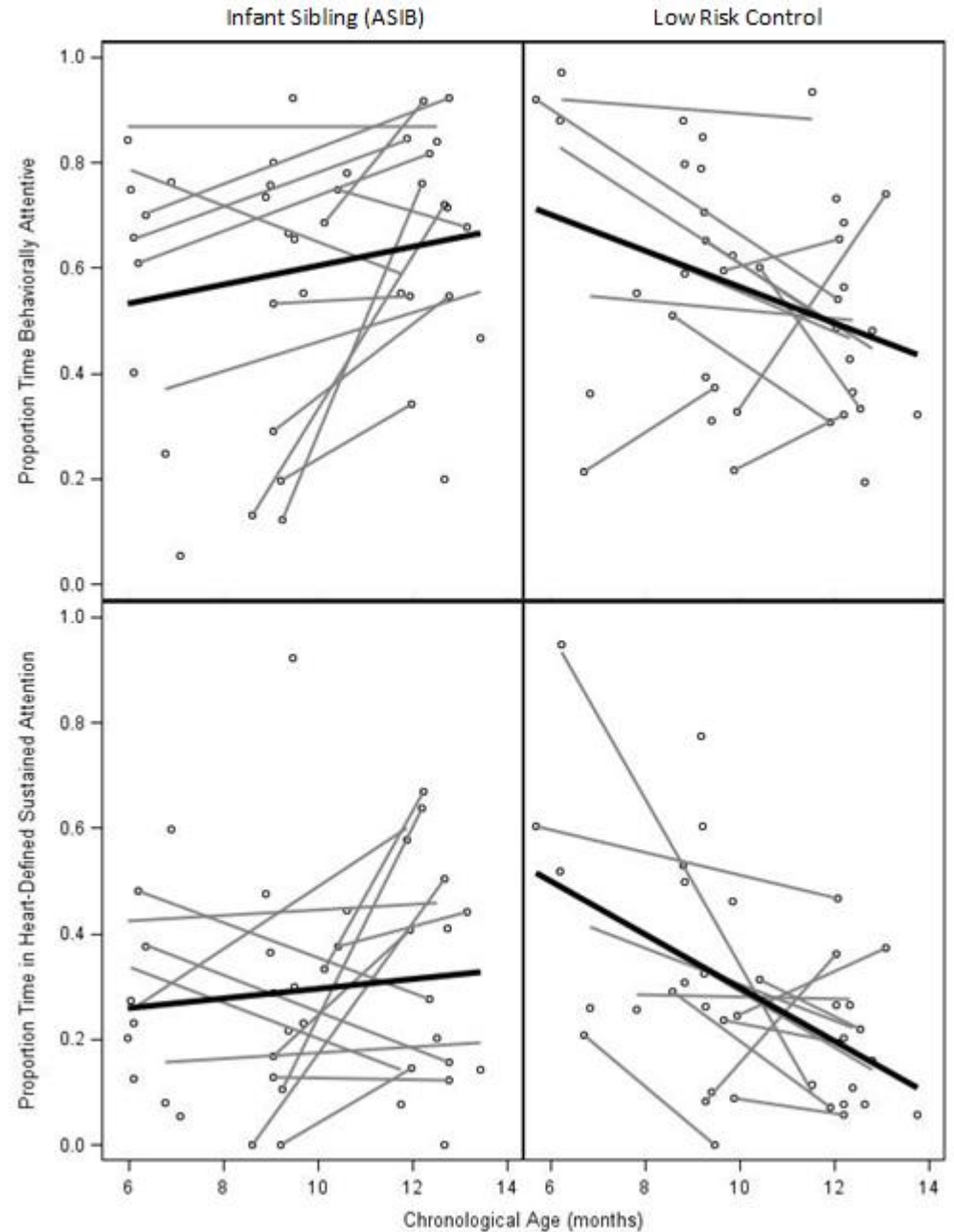
## **BIOBEHAVIORAL ASSOCIATIONS**

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behavioral and sustained  
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# Results

## CROSS-GROUP DIFFERENCES

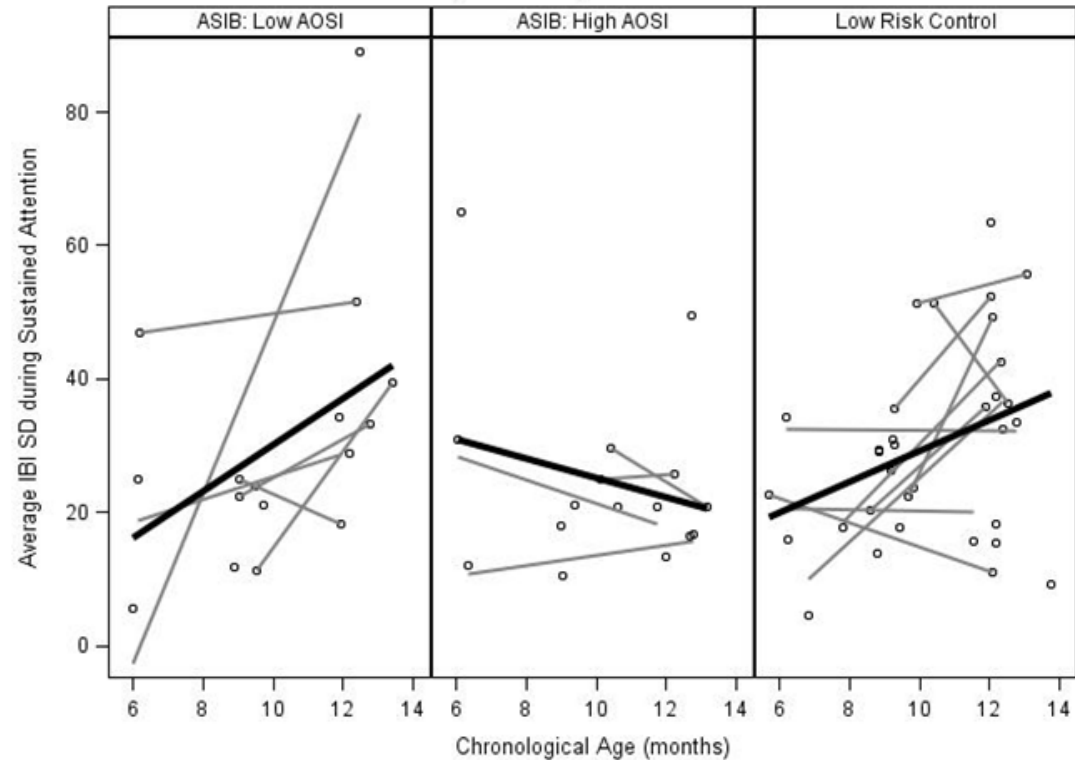
ASIBs failed to display typical decreases of behavioral and sustained attention across age



# Results

## CLINICAL SIGNIFICANCE

Physiological variables predicted clinical ASD risk



- Among ASIBs with AOSI data (n=19; 39 assessments), higher clinical autism risk associated with abnormal trajectories of:
  - Global IBI (overall IBI, IBI SD)
  - Sustained attention (IBI change, IBI variability)
- Behavioral variables *ns*



# Summary

- Abnormal arousal present in infancy in ASIBs, prior to onset of autism symptomatology
- Substantial heterogeneity in profiles

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**Predicted  
ASD Risk**

# DISCUSSION

# Take-Home Points

## **BIOBEHAVIORAL ASSOCIATIONS**

Proportion of time in behavioral attention correlated with proportion of time in SA, but not SA features

## **CROSS-GROUP DIFFERENCES**

Abnormal behavioral and heart-defined attention emerged within the first year of life in ASIBs

## **CLINICAL SIGNIFICANCE**

Abnormal physiological profiles (not behavior) predicted clinical ASD risk

# 3 Key Outcomes:

- Supports abnormal orienting as
  - Endophenotype of ASD
  - Potential predictor of clinical risk
- Deficits may be emerging earlier than previously reported
  - Longitudinal methods revealed nuanced changes
  - Further work needed to establish longitudinal outcomes
- Heart activity – not behavior – sensitive to within-group risk
  - SA as potential biomarker
  - Increased sensitivity to growth – treatment monitoring?

# Limitations & Next Steps

## Limitations:

- Underpowered to examine sex and nuanced age effects
- G-O task design
- Lack of outcome data

## Next Steps:

- Examine outcomes (ASD, developmental, language, anxiety)
- Examine additional indicators of attention
- Design tasks to test visual processing versus arousal  $H_0$

# Long-Term Impact

- Inform early detection, prevention and intervention
- Improve diagnostic tools in NDDs
- Promote school readiness
- Support families and teachers

“For the first time, ***prevention*** of ASD is plausible. Prevention will entail detecting infants at risk before the full syndrome is present and implementing treatments designed to alter the course of early behavioral and brain development.”

- Geraldine Dawson (2008)



# Thank you!

- Our wonderful participants
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  - Claire Harryman
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  - Erica Mazur
  - Bailey Tackett
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