The Onset Of Autism During Infancy

Insights From Sibling Studies

UCLA CART
CENTER FOR AUTISM RESEARCH AND TREATMENT

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The Help Group Summit 2012

Autism Spectrum Disorders

A. Social interaction
- Eye contact, facial expression
- Peer relationships
- Sharing interest and enjoyment
- Social/emotional reciprocity

B. Communication
- Language, conversation, echolalia
- Play

C. Restricted & Repetitive Behaviors
- Restricted interests/preoccupations,
- inflexible adherence to routines, stereotypies

Autism Prevalence

- Nationwide: 1/88 = 1.1% (CDC, 2012)
- Boys are 4-5 times more likely to be affected with autism than girls

Age at Diagnosis

- Autistic Disorder (general population) 3.1 years
- PDD-NOS 3.9 years
- Asperger's Disorder 7.2 years
- Autistic Disorder (African American children) 7.9 years

Timing of Diagnosis

- Diagnoses are typically not made before the fourth year (Mandell et al., 2005)
- Outcomes are improved for children who receive early intervention (Bibby et al., 2002; Goldstein, 2002; Harris & Handleman, 2000; Lord, 2001; Rogers, 1998)
- Diagnoses conferred prior to 30 months are not as stable as those conferred after 30 months (Turner & Stone, 2007)

Reasons to Study Infants

- Early Detection
  - Channel children into treatment
- Treatment
  - What features, symptoms, skills to target
- Advance the study of autism
  - Characterize onset patterns
  - Inform genetic, neurobiological research

Studying Infant Siblings

- Autism is highly heritable

  (Bailey et al., 1995; Steffenburg et al., 1989)

- Recurrence rates within families estimated at 18.8%. 26.2% for boys. 32.2% in multiplex families.

  (Ozonoff et al., 2011)

Recruitment Groups

High-Risk Group	Infant siblings of children with autistic disorder
Low-Risk Group	Infants with no family history of developmental disabilities

“Outcome” Groups

High-Risk Group (Infant Siblings)	Sibs-ASD
	Sibs-Concerns
	Sibs-TD
Low-Risk Group	Low-Risk TD

Initiating Joint Attention

(Rozga et al., 2011)

Response to Examiner's Bids for Joint Attention

(Rozga et al., 2011)

Requesting

(Rozga et al., 2011)

J Autism Dev Disord (2011) 41:287–301
DOI 10.1007/s10803-010-1051-6

ORIGINAL PAPER

Behavioral Profiles of Affected and Unaffected Siblings of Children with Autism: Contribution of Measures of Mother–Infant Interaction and Nonverbal Communication

Agata Rozga · Ted Hutman · Gregory S. Young · Sally J. Rogers · Sally Ozonoff · Mirella Dapretto · Marian Sigman

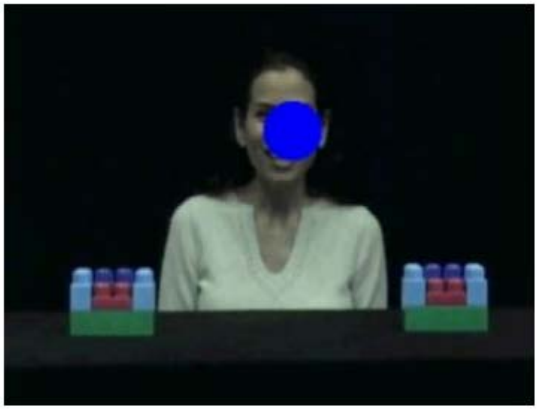
- No differences in mother/infant behaviors at 6 mos.
  - Social gaze, vocalization, smiles
- 12-month non-verbal communication:
  - Pointing/showing
  - Response to pointing
  - Requesting

Joint Attention in the Eye-Tracker

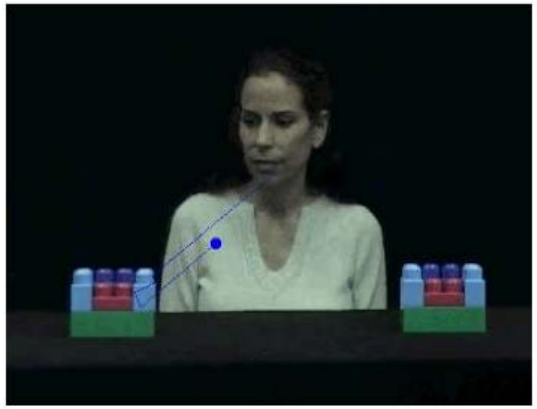
Kristen Gillespie-Lynch

Attention Getter

Baseline

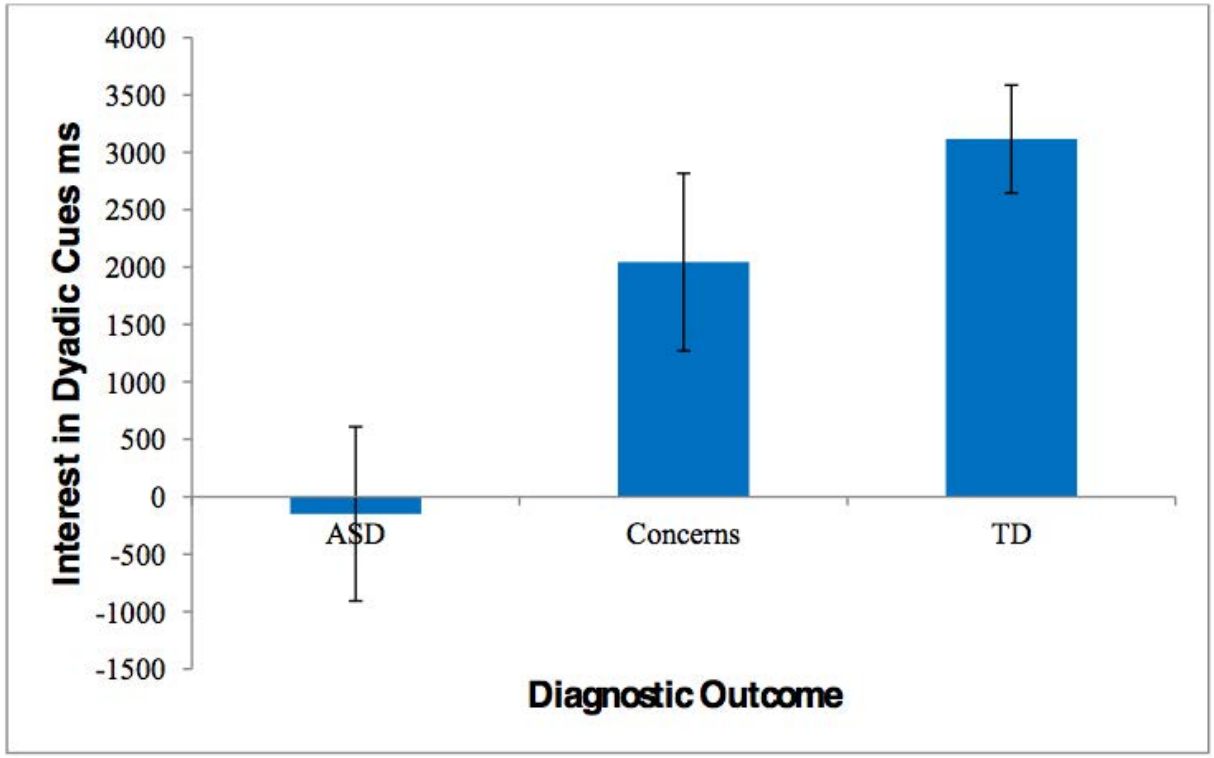


Social Greeting



Opportunity for Gaze Following

Response to Social Greeting

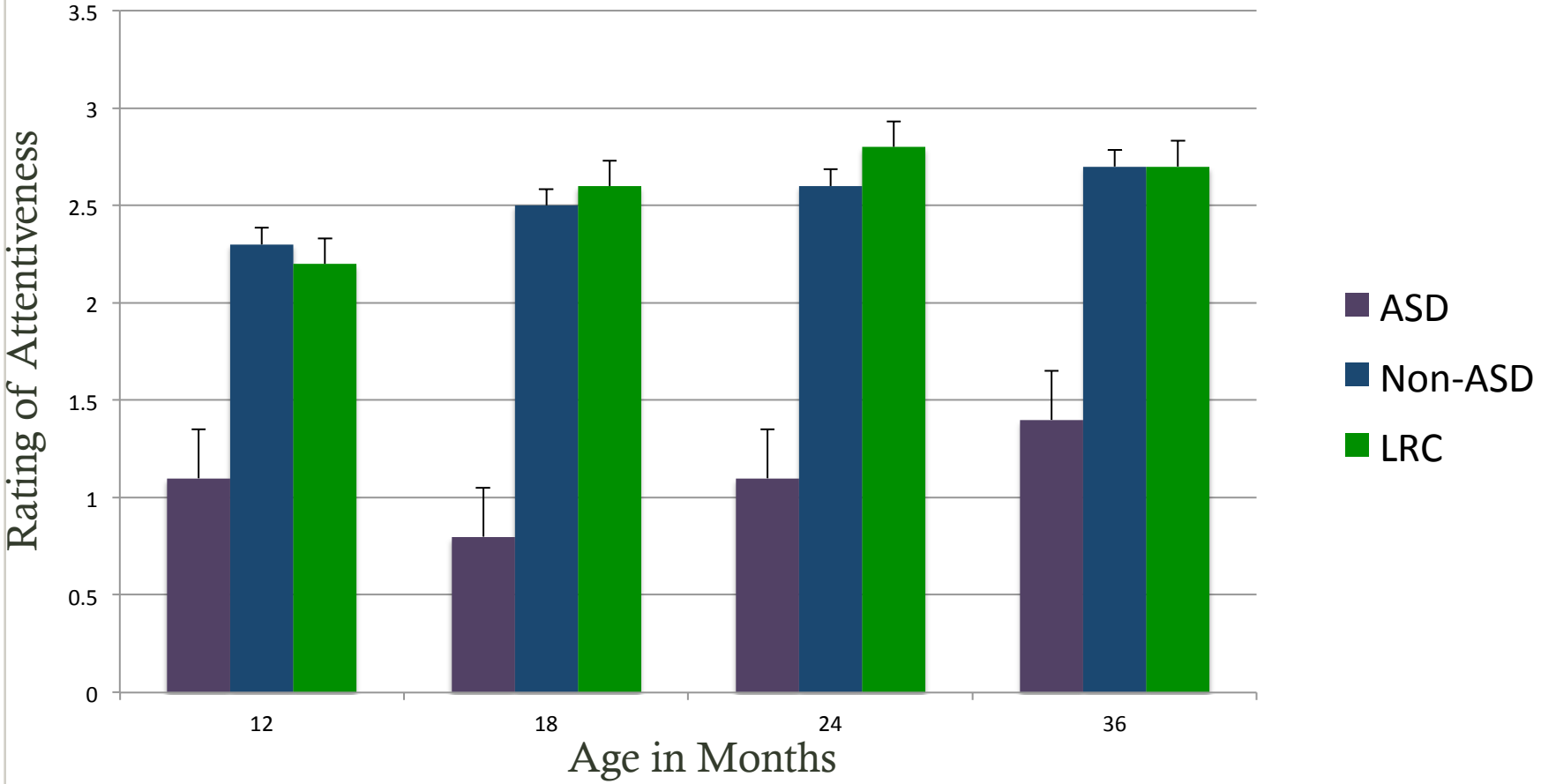


$F(1, 18) = 6.295; p = .008$

Response to Another Person's Distress

Attention to Distress

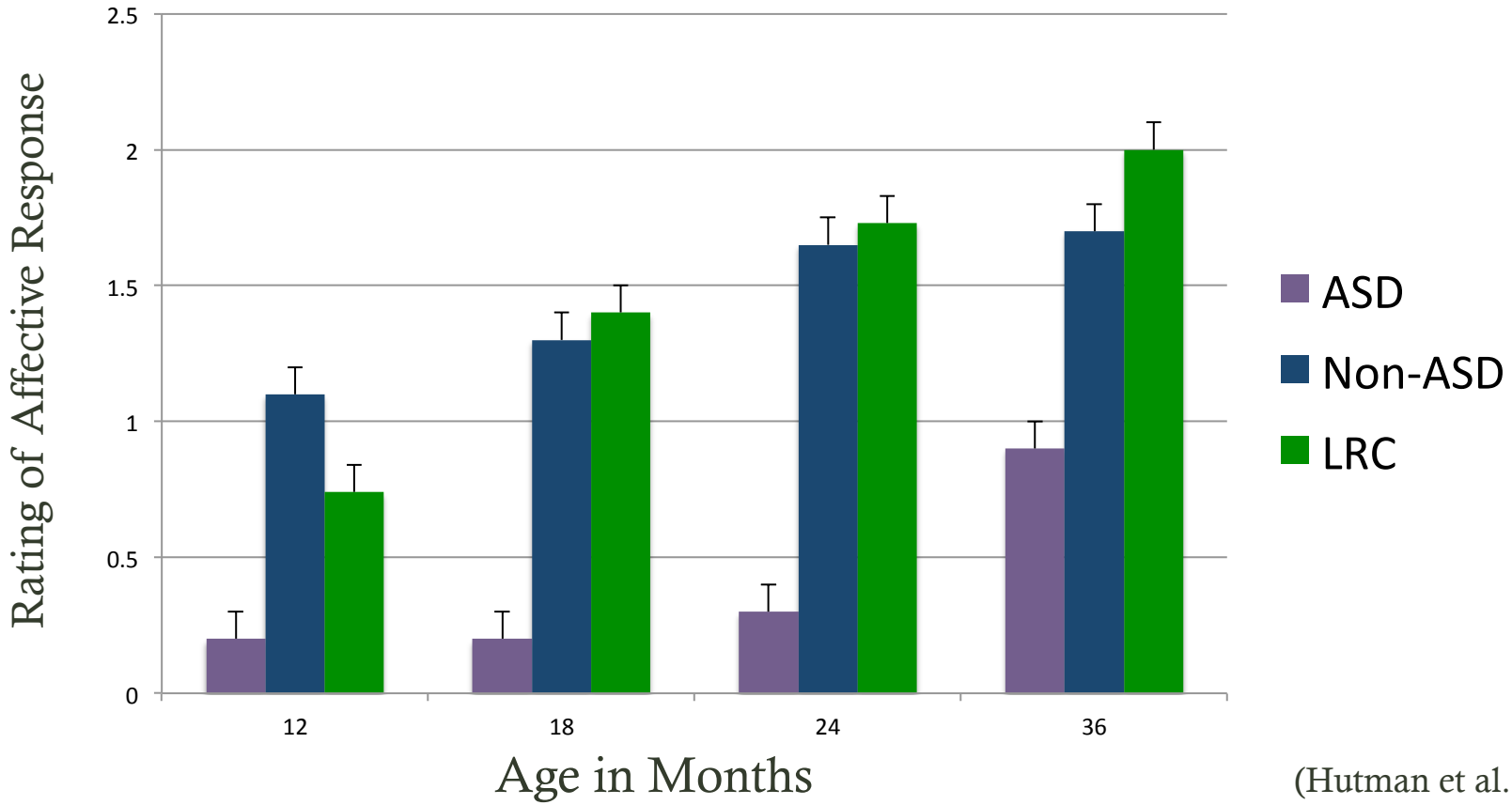
(12, 18, 24, 36 months)



(Hutman, Rozga, DeLaurentis, Barnwell, Sugar, & Sigman, *JCPP*, 2010)

Affective Response to Distress

(12, 18, 24, 36 months)



(Hutman et al., 2010)

J Autism Dev Disord (2012) 42:487–498
DOI 10.1007/s10803-011-1262-5

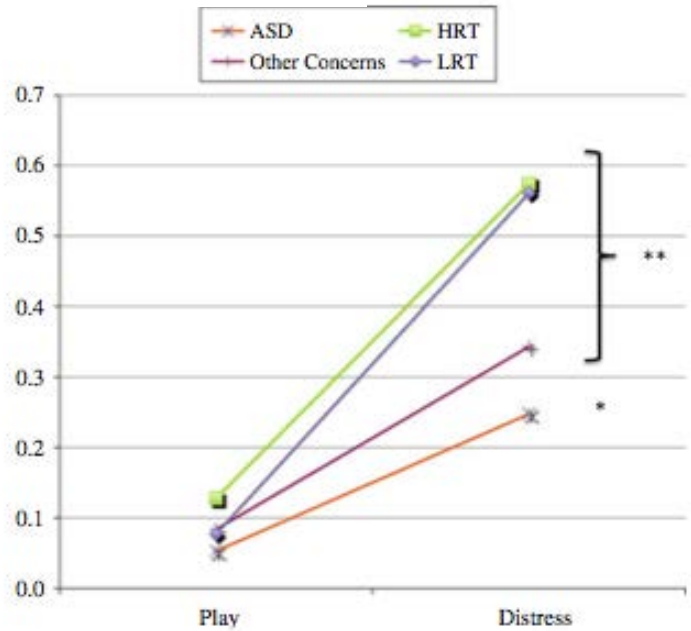
ORIGINAL PAPER

Selective Visual Attention at Twelve Months: Signs of Autism in Early Social Interactions

Ted Hutman · Mandeep K. Chela · Kristen Gillespie-Lynch · Marian Sigman

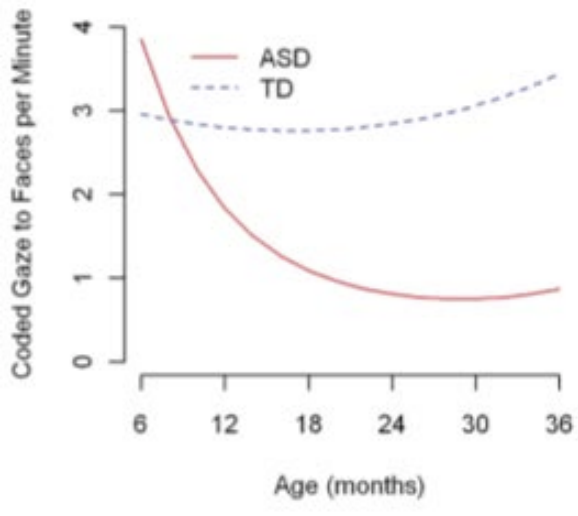
- Awareness of change in social context
- Attentiveness to examiner
- Differences in duration of attention

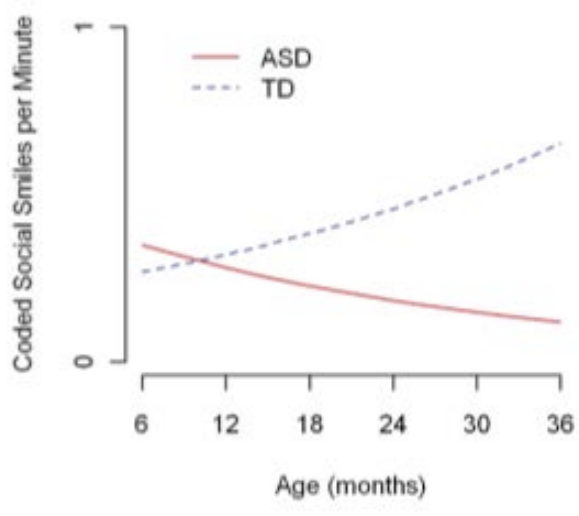
  as well as number of gaze shifts
- Early evidence of BAP?

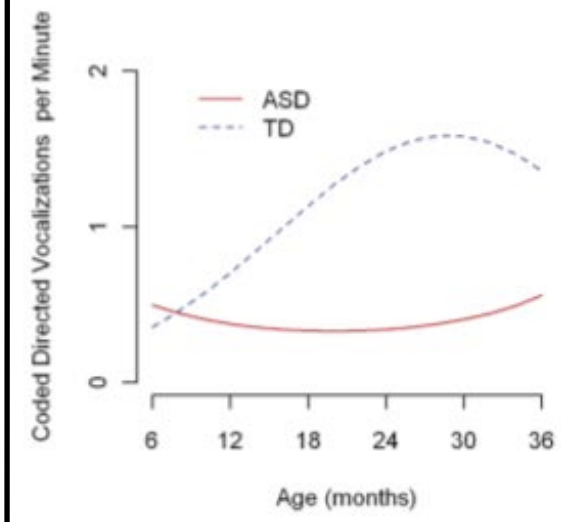


Social Behavior During Cognitive Testing

Social Behavior During Cognitive Testing







Gaze to Face | Social Smile | Directed Vocalization

(Ozonoff et al., *JACAAP*, 2010)

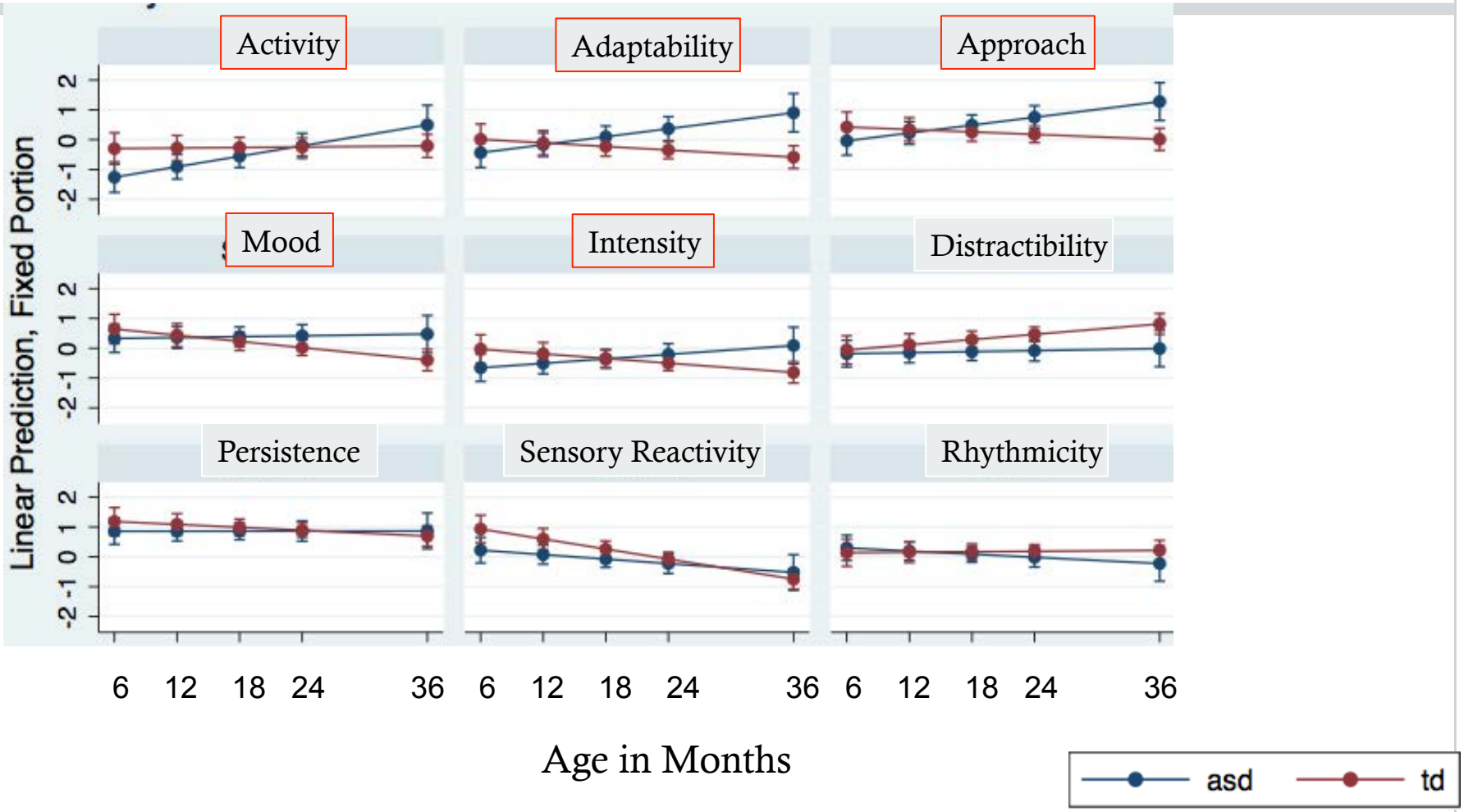
How Early Do Parent Concerns Predict Later Autism Diagnosis?

(J Dev Behav Pediatr 30:367–375, 2009)

Sally Ozonoff, PhD,* Gregory S. Young, PhD,* Mary Beth Steinfeld, MD,* Monique M. Hill, MS,* Ian Cook, PhD,* Ted Hutman, PhD,† Suzanne Macari, PhD,‡ Sally J. Rogers, PhD,* Marian Sigman, PhD†

- Parents of children with autism are aware of the risk to later-born infants and report more general developmental concerns about the infants at study intake (6 months)
- At and after 12 months, parental concerns are more specific to ASD-related symptoms and are useful predictors of which high-risk infants will go on to receive a diagnosis at 36 months

Longitudinal Parent Report on Child Temperament



Parent-reported Temperament Trajectories

Mithi del Rosario & Kristen Gillespie-Lynch

- Trajectories of Sibs-ASD differed from Sibs-TD
  - *Increasing* activity levels, negative affect, and intensity of affective responses
  - *Decreasing* adaptability and approach behaviors
- Links between parent-reported temperament at 12 months and parent behaviors during mother-child free play interaction at 18 months.

Motor Skills Development

with Shafali Jeste, MD

Table 1 Domains of impairment in autistic spectrum disorder (ASD)[a]

Domain	Autism	Asperger	PDD-NOS	ASD
social communication	required	required	required	
language	required	–	variable	
repetitive, restrictive behaviors	required	required	variable	
sensory abnormalities	>90%	80%	variable	94%
developmental regression[b]	15%–40%	?	?	15%–40%
motor signs[c]	60%–80%	60%	60%	60%–80%
gross motor delay	10%	?	?	5%–10%
sleep disturbance	55%	5%–10%	40%	50%
gastrointestinal disturbance[d]	45%	4%	50%	4%–50%
epilepsy[e]	10%–60%	0%–5%	5–40%	6%–60%
comorbid psychiatric diagnosis[f]	70%	60%	>25%	25–70%

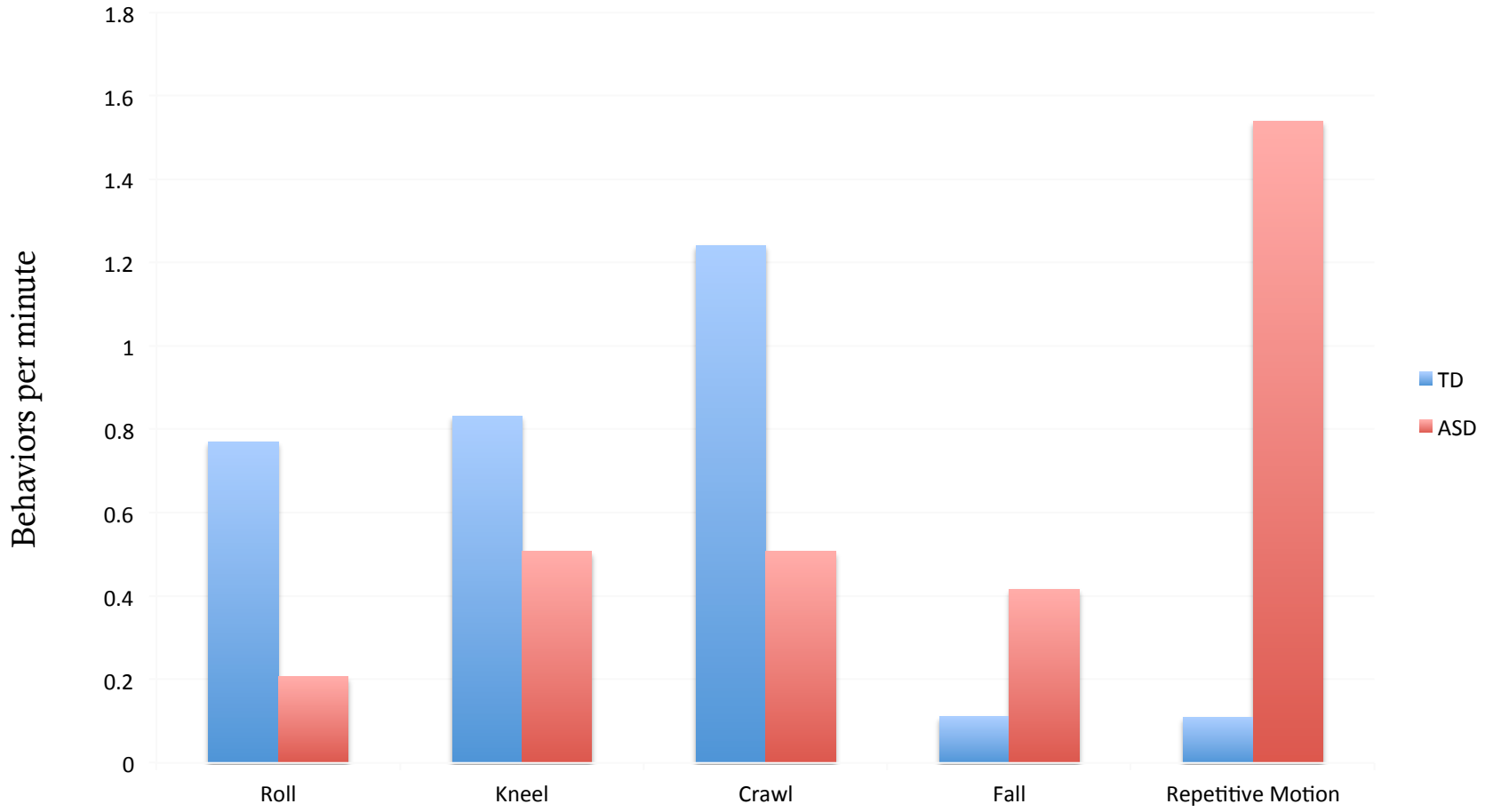
(Geschwind, *Ann Rev Med,* 2009)

Motor Skills Development
with Shafali Jeste, MD

- Raw scores on Mullen Gross Motor Scale at 6 months are normally distributed
- 6-month gross motor scores are correlated with the following measures at 12 months:
  - Receptive Language, $r = .31$, $p = .01$
  - Visual Reception, $r = .29$, $p = .02$
  - Requesting (ESCS), $r = .30$, $p = .04$

Motor Behavior at 12 months

Motor Behavior at 12 months



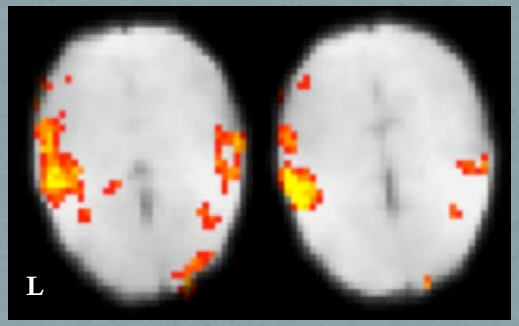
Combining the Warning Signs

- Using the following predictors at 12 months:
  - Response to name
  - Joint Attention
  - Language skills
  - Selective attention to social stimuli
- Selects a group for whom the estimated probability of ASD diagnosis is 47.1%

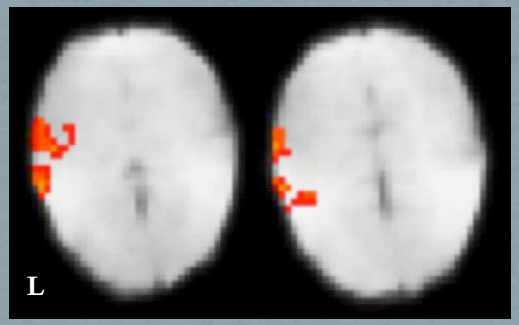
The Search for Early Biomarkers of ASD

6-week-old (passive fMRI)

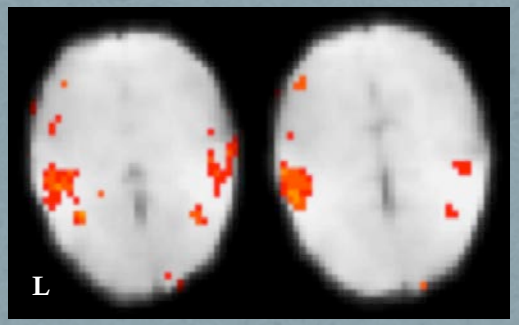
English > Rest



Japanese > Rest

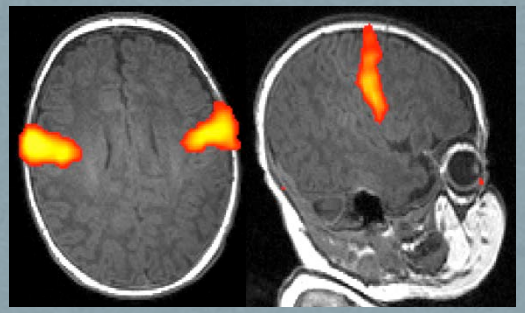


English > Japanese

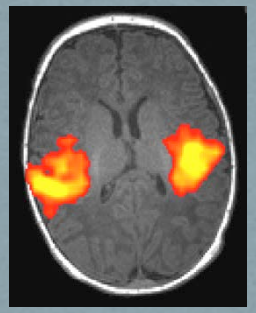


8-week-old (rs-fcMRI)

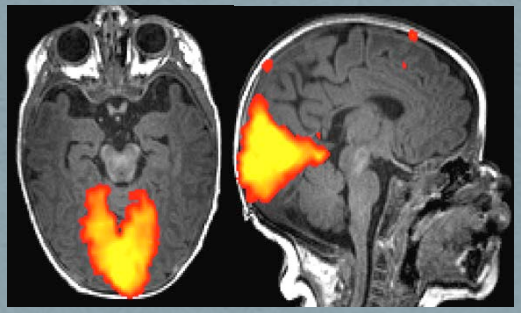
Sensorimotor Network



Auditory Network



Visual Network



Salience Network

Eye movement and pupillometry

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NOW ENROLLING

- Infants < 6 weeks of age
  - 2 older siblings with ASD, OR
  - 1 older sibling + family history of ASD
  - Control group: NO family history of ASD
- Referral to **free treatment study** for eligible participants

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