Increasing access to early diagnosis and assessment of autism via objective and cost-effective eye-tracking-based tools

On the crisis of limited access to early diagnostic services

an ongoing journey …

2025 Meet The Scientist Webinar Series
Brain & Behavior Research Foundation
February 11, 2025

Ami Klin, PhD
Director, Marcus Autism Center, Children's Healthcare of Atlanta
Georgia Research Alliance Eminent Scholar
The Bernie Marcus Distinguished Chair in Autism
Professor and Chief, Division of Autism & Related Disabilities,
Department of Pediatrics,
Emory University School of Medicine
Emory Center for Translational Social Neuroscience

General Disclosures

Warren Jones, PhD

- This presentation includes research related to device development.
- Drs. Klin and Jones are inventors and patent holders of medical device technologies licensed in 2020 to EarliTec Diagnostics.
- EarliTec is a company that develops technologies for early identification and treatment monitoring in autism, and gives revenue to support treatment of children with autism. Dr. Klin and Jones are scientific consultants to and equity holders in EarliTec Diagnostics. Majority ownership is by Children's Healthcare of Atlanta, a non-profit, with the commitment of returning investment into treatment of autism.
- Drs. Klin and Jones' external activity with EarliTec Diagnostics has been reviewed and approved by Emory University's Conflict of Interest Review Office and by Emory University School of Medicine's Dean's Office.
- Drs. Jones and Klin's research has been supported by grants from NIMH, NICHD, NIBIB, SFARI, the Marcus Foundation, the JB Whitehead Foundation, and the Autism Science Foundation.

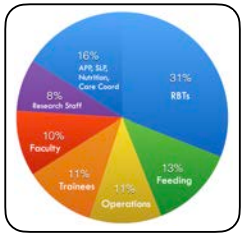
My personal story … and the gold standards

- 1990-2010 Yale Child Study Center, Yale School of Medicine
- 2011-2024 Marcus Autism Center, Emory School of Medicine and Children's Healthcare of Atlanta

Marcus Autism Center

532 staff

5 locations



2023

Provided 45,764 visits (6% increase)

6,397 unique children served (7% growth)

Community Partners

The need:

Challenges we collectively face

The gold standard is not accessible

~ 100,000 children are born every year …. Early intervention ….

1 in 5 is diagnosed before age 3

Median age 4.3-5.5 years

Access to exp

PEDIATRICS

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

The Diagnostic Odyssey of Autism Spectrum Disorder

Martine Lappé, PhD,[a] Lynette Lau, PhD,[b,c] Rebecca N. Dudovitz, MD, MSHS,[c] Bergen B. Nelson, MD, MSHS,[d] Elizabeth A. Karp, MS,[e] Alice A. Kuo, MD, PhD, MBA[b,c]

An Illustration from Georgia

DPH Georgia Department of Public Health

Early Intervention Because Babies Can't Wait BCW

Is this acceptable,
is it ethical,
and is it equitable?

In regard to African American children with autism

John Constantino MD

- AA children (and Latino children) with ASD, on average, ar… er, are more likely to have carried non-ASD diagnose… healthcare services, and are less likely to h…

Black children with autism have double the risk of intellectual disability than White children with autism

- Constantino, Abbacchi … …rican American Children", *Pedi…* …By Pediatrics editorial on struct… …cess to developmental services
  - …story of diagnosis and phenotypic information … with ASD (N=584) - Event History Calendar Interviews
  - …age age of ASD diagnosis was 64.9 months (+/- 49.6), on average 42.3 months (+/- 45.1) following parents' first concerns about their children's development
    - Age Parental First Concerns: 23.0 (17.9)
    - Age Parent First Shared Concerns with a Professional: 29.1 (23.1)

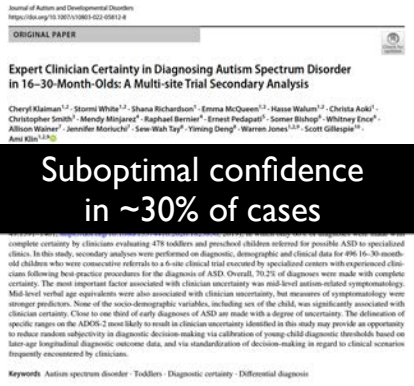
The purpose of diagnostics in medicine

NATIONAL ACADEMIES Sciences Engineering Medicine

The committee concluded that improving the diagnostic process is not only possible, but also represents a moral, professional, and public health imperative.

And the gold standard is at times "silverish"

Clinician confidence in diagnosis of toddlers



Journal of Autism and Developmental Disorders
https://doi.org/10.1007/s10803-022-05812-8

ORIGINAL PAPER

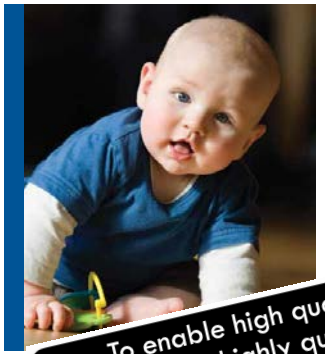
Expert Clinician Certainty in Diagnosing Autism Spectrum Disorder in 16–30-Month-Olds: A Multi-site Trial Secondary Analysis

Cheryl Klaiman[1,2] · Stormi White[1,2] · Shana Richardson[1] · Emma McQueen[1,2] · Hasse Walum[1,2] · Christa Aoki[1] · Christopher Smith[1] · Mendy Minjarez[4] · Raphael Bernier[4] · Ernest Pedapati[4] · Somer Bishop[4] · Whitney Ence[4] · Allison Wainer[4] · Jennifer Moriuchi[4] · Sew-Wah Tay[4] · Yiming Deng[4] · Warren Jones[1,2,4] · Scott Gillespie[1,2] · Ami Klin[1,2,4]

Suboptimal confidence in ~30% of cases

Klaiman et al. (2024) *JADD*.

Diagnostic and treatment biomarkers are sorely needed in autism

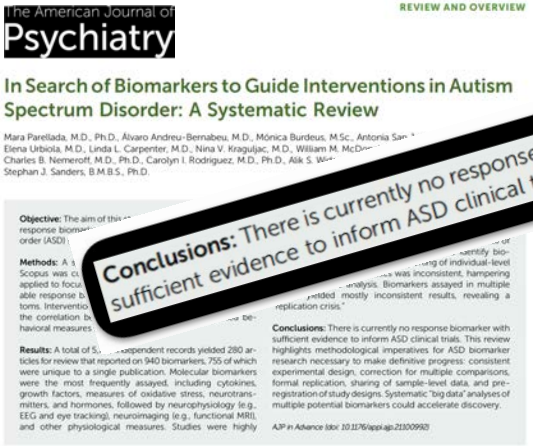


Need measures that are

- objective
- quantitative
- dimensional & fine-grained
- performance-based
- standardized, efficient & community-viable
- able to capture core [illegible] social [illegible]

To enable high quality early diagnosis via objective, standardized, highly quantitative, and cost-effective technology leveraging developmental social neuroscience

The current state



The American Journal of Psychiatry

REVIEW AND OVERVIEW

In Search of Biomarkers to Guide Interventions in Autism Spectrum Disorder: A Systematic Review

Mara Parellada, M.D., Ph.D., Álvaro Andreu-Bernabeu, M.D., Mónica Burdeus, M.Sc., Antonia San[illegible], Elena Urbiola, M.D., Linda L. Carpenter, M.D., Nina V. Kraguljac, M.D., William M. McDo[illegible], Charles B. Nemeroff, M.D., Ph.D., Carolyn I. Rodriguez, M.D., Ph.D., Alik S. Wei[illegible], Stephan J. Sanders, B.M.B.S., Ph.D.

Objective: The aim of this [illegible] response biom[illegible] order (ASD) [illegible]

Methods: A [illegible] Scopus was c[illegible] applied to focu[illegible] able response b[illegible] toms. Interventio[illegible] the correlation b[illegible] havioral measures [illegible]

Results: A total of 5[illegible] independent records yielded 280 articles for review that reported on 940 biomarkers, 755 of which were unique to a single publication. Molecular biomarkers were the most frequently assayed, including cytokines, growth factors, measures of oxidative stress, neurotransmitters, and hormones, followed by neurophysiology (e.g., EEG and eye tracking), neuroimaging (e.g., functional MRI), and other physiological measures. Studies were highly [illegible] of individual-level [illegible] was inconsistent, hampering [illegible] analysis. Biomarkers assayed in multiple [illegible] yielded mostly inconsistent results, revealing a [illegible] replication crisis."

Conclusions: There is currently no response biomarker with sufficient evidence to inform ASD clinical trials. This review highlights methodological imperatives for ASD biomarker research necessary to make definitive progress: consistent experimental design, correction for multiple comparisons, formal replication, sharing of sample-level data, and preregistration of study designs. Systematic "big data" analyses of multiple potential biomarkers could accelerate discovery.

AJP in Advance (doi: 10.1176/appi.ajp.21100992)

Conclusions: There is currently no response biomarker with sufficient evidence to inform ASD clinical trials.

The bible of diagnostic clinical trials: from 1999

JAMA The Journal of the American Medical Association

Empirical Evidence of Design-Related Bias in Studies of Diagnostic Tests

Jeroen G. Lijmer, MD
Ben Willem Mol, MD, PhD
Sieni Heisterkamp, PhD
Gouke J. Bonsel, MD, PhD
Martin H. Prins, MD, PhD
Jan H. P. van der Meulen, MD, PhD
Patrick M. M. Bossuyt, PhD

Context The literature contains a large number of potential biases in the evaluation of diagnostic tests. Strict application of appropriate methodological criteria would in... validate the clinical application of most study results.

Objective To empirically determine the quantitative effect of ... comings on estimates of diagnostic accuracy.

Design and Setting Observational studies ... nal studies evaluating 218 diagnostic ... identified through a systematic ... DARE database ...

BMJ Open ...

... Douglas G Altman,[3] David E Bruns,[4] ... Les Irwig,[7] Deborah Levine,[8,9] ... Henrica C W de Vet,[11] Patrick M M Bossuyt[1]

STARD (STANDARDS FOR REPORTING OF DIAGNOSTIC ACCURACY STUDIES)

The STARD statement (Standards for Reporting of Diagnostic Accuracy Studies) was developed to improve the completeness and transparency of reports of diagnostic accuracy studies.

Word of warning: reading diagnostic studies using MACHINE LEARNING OR DEEP LEARNING

JAMA The Journal of the American Medical Association

VIEWPOINT

Challenges to the Reproducibility of Machine Learning Models in Health Care

The "black box"

Andrew L. Beam, PhD
Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, Massachusetts; and Department of Biomedical Informatics, Harvard Medical School, Boston, Massachusetts.

Arjun K. Manrai, PhD
Department of Biomedical Informatics, Harvard Medical School ...

Reproducibility has been an important and intensely debated topic in science and medicine for the past few decades.[1] As the scientific enterprise has grown in scope and complexity, concerns regarding how well new findings can be reproduced and validated across different scientific teams and study populations have emerged. In some instances,[2] the failure to replicate numerous previous studies has added to the growing concern that science and biomedicine may be in the midst of a "reproducibility crisis." Against this backdrop, ... chine learning models are ... successes in ...

Unique Challenges to Reproducibility Posed by Machine Learning

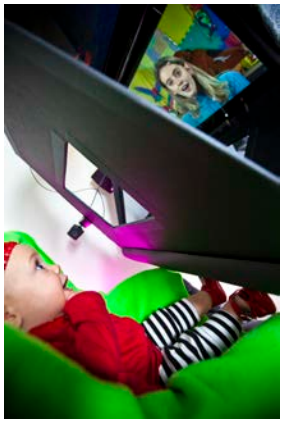
... researchers ... versions of a software ... substantially different conclusions if ... tant parameters are given different values.

The training of many machine learning models makes use of randomness, and this is especially true for deep learning models,[3,4] which are trained by a process known as stochastic gradient descent. As the name implies, the model is updated using a randomized procedure that will result in different final values for the model parameters ev-

... of Science, Engi- ... rst, it is important to distinguish ... notions of reproducibility and replication. A study is reproducible if, given access to the underlying data and analysis code, an independent group can obtain the

Our biomarker

Eye-tracking measures of SOCIAL VISUAL ENGAGEMENT



how children look at and learn from their surrounding social environment

- At a rate of 120 times/second

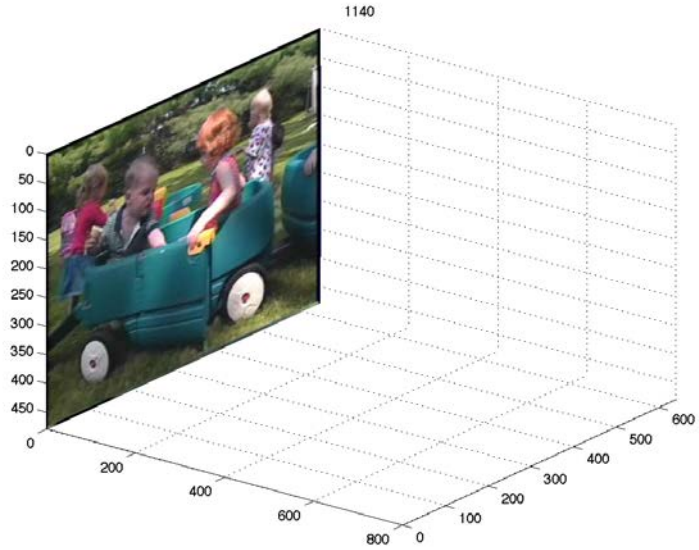
Jones & Klin (2013) *Nature*.

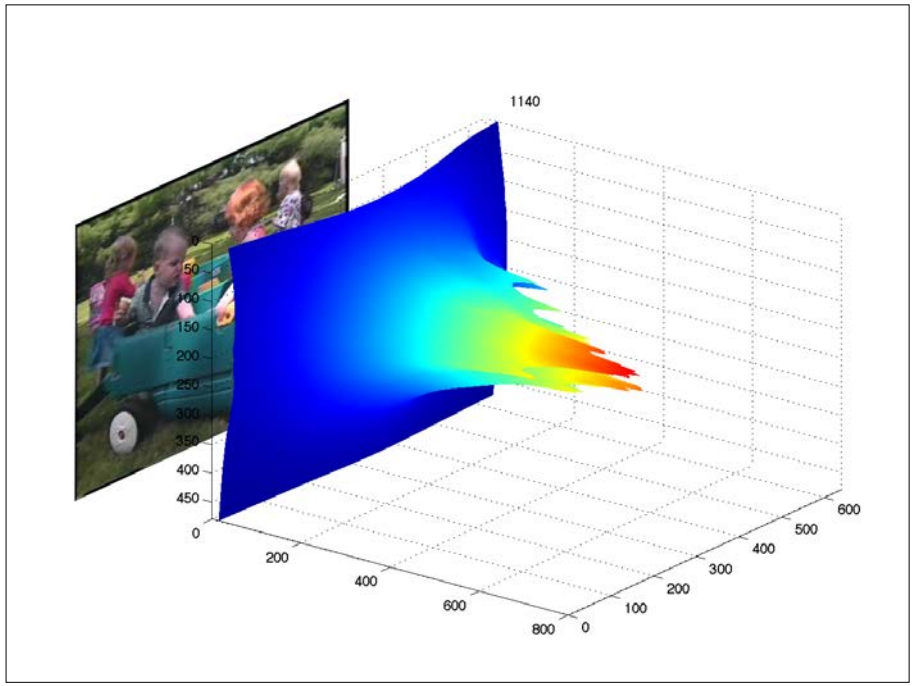
Social Visual Engagement, moment-by-moment

+

Individual eye-tracking data, playback 1/2 speed, gaze location crosshair color-coded by content at gaze location.

Quantifying social visual engagement, moment-by-moment

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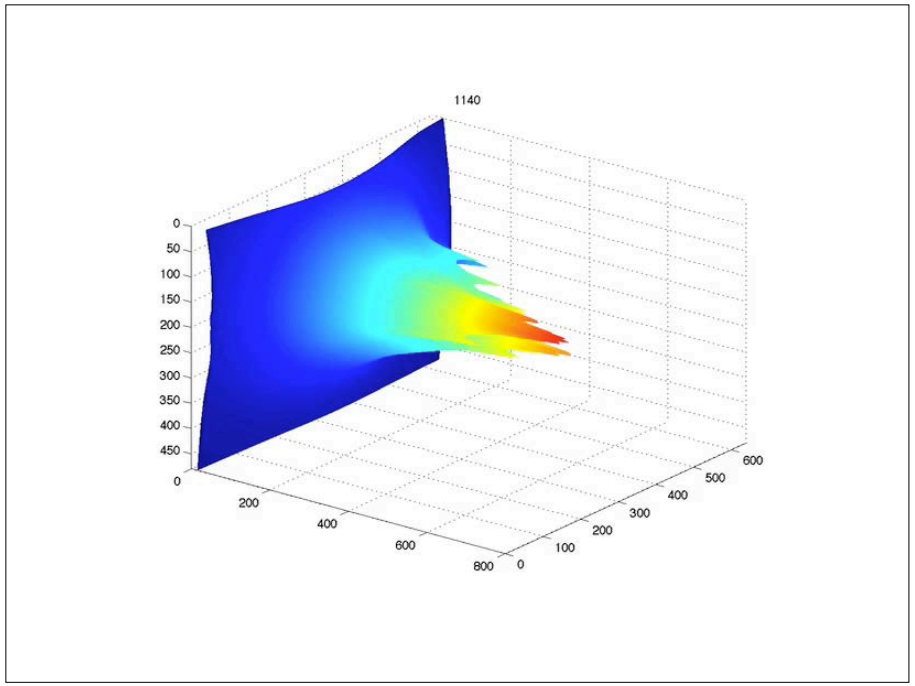
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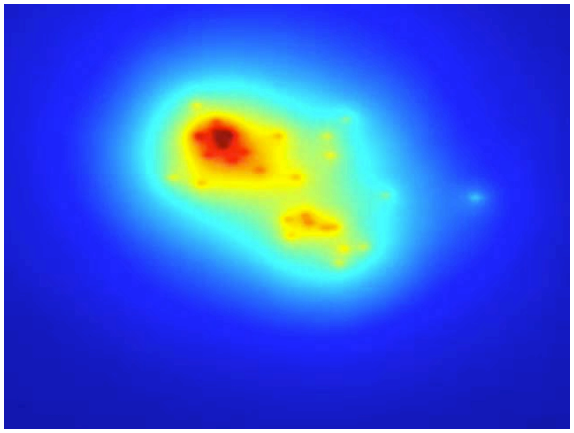

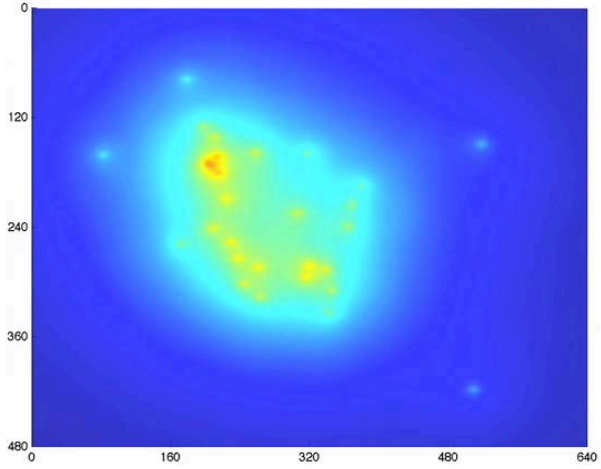
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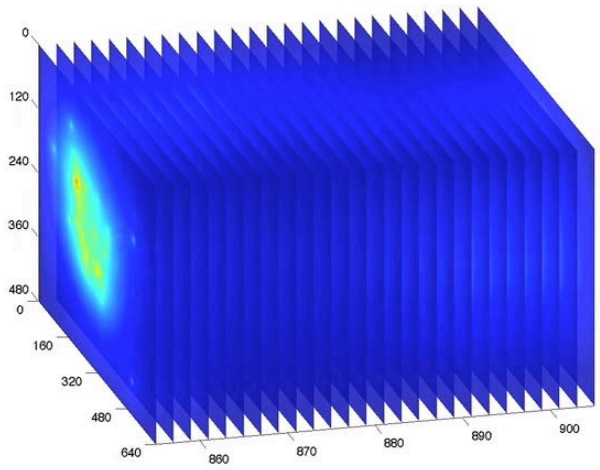
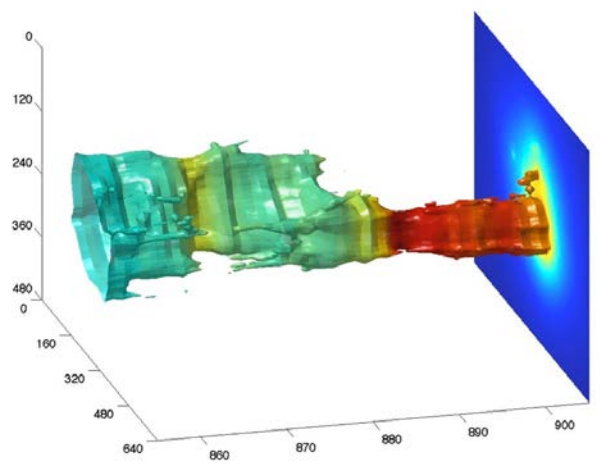


Quantification: Attentional Funnel



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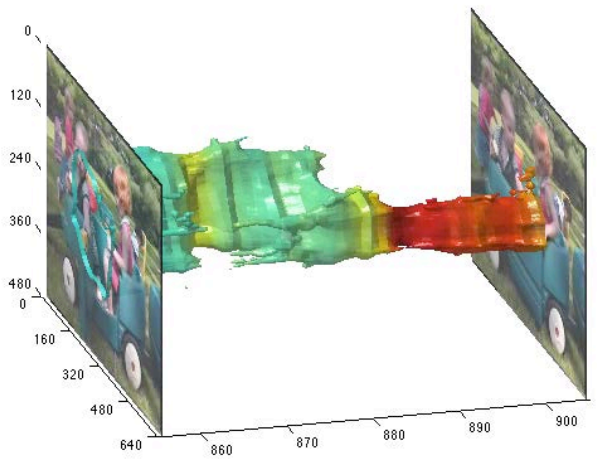
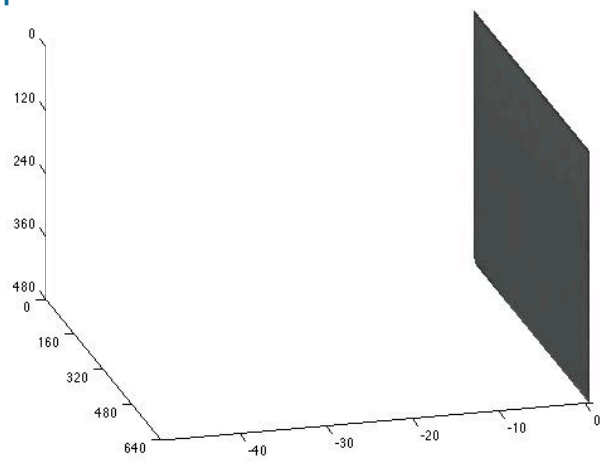
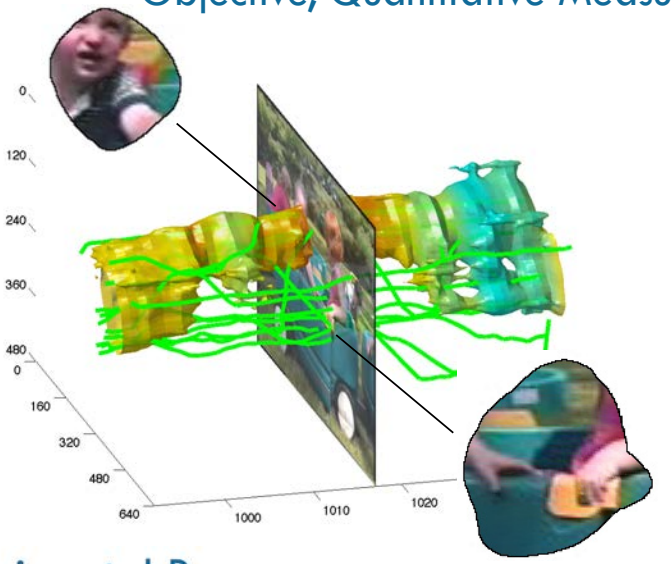


Moment-by-moment entrainment to "hot spots" of socialization

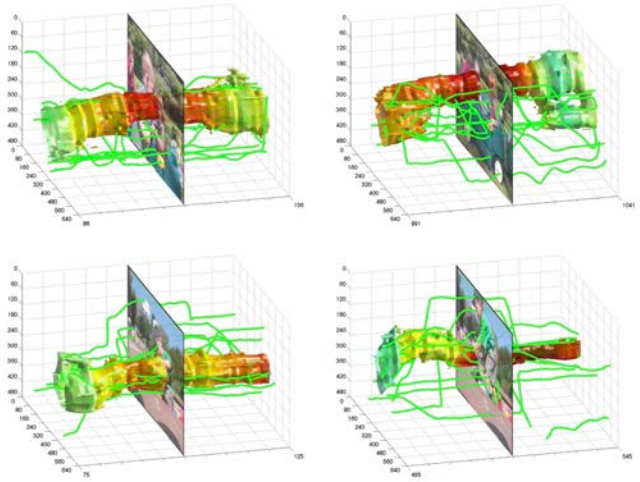


Objective, Quantitative Measures

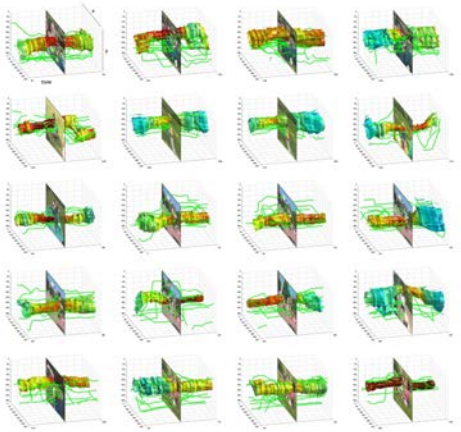


Experimental Presses

Hundreds and hundreds of Experimental Presses within a few minutes of video watching



Thousands of natural experiments within a 10-minute video experiment



✶ In autism: 1,000s of divergences in 10-12 minutes of video

TD normative funnels =

ASD comparison scanpaths =

Performance-Based Measures of Strengths and Vulnerabilities

Example: Pointing & Social Monitoring

Environmental Context

Performance-Based Measures of Strengths and Vulnerabilities

Example: Pointing & Social Monitoring

Quantitative Reference Metric: Age-Expected Social Visual Engagement

Performance-Based Measures of Strengths and Vulnerabilities

Performance-Based Measures of Strengths and Vulnerabilities

Example: Facial Affect

Environmental Context

Performance-Based Measures of Strengths and Vulnerabilities

Example: Facial Affect

Quantitative Reference Metric: Age-Expected Social Visual Engagement

Performance-Based Measures of Strengths and Vulnerabilities

The science behind the biomarker

>20 years of research

Marcus AUTISM CENTER

Autism symptoms RESULT from deviations from normative socialization

Genetics → Autism

Jones et al. (2008). *Arch Gen Psy* / Klin et al. (2009). *Nature* / Jones & Klin (2009). *J Am Acad of Child Psy* / Jones & Klin (2013). *Nature* / Klin et al. (2014). *Neurosci Biobehav Rev* / Moriuchi et al. (2017). *Am J Psy* / Constantino et al. (2017). *Nature* / Shultz et al. (2018). *TICS* / Klin et al. (2020). *Dev & Psychopathol*

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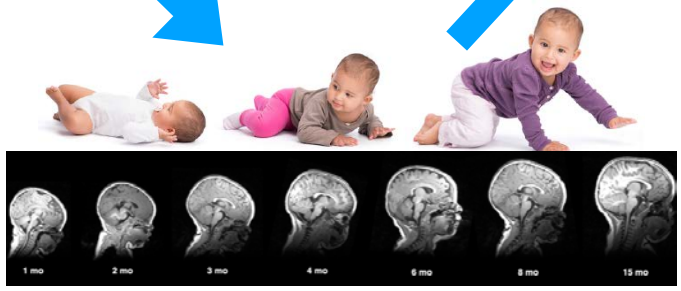


Normative Behavior & Brain Development

Jones et al. (2008). *Arch Gen Psy* / Klin et al. (2009). *Nature* / Jones & Klin (2009). *J Am Acad of Child Psy* / Jones & Klin (2013). *Nature* / Klin et al. (2014). *Neurosci Biobehav Rev* / Moriuchi et al. (2017). *Am J Psy* / Constantino et al. (2017). *Nature* / Shultz et al. (2018). *TICS* / Klin et al. (2020). *Dev & Psychopathol*

The beginning

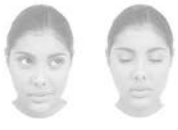
Neonates preferentially orient towards stimuli that…

More Preferred

mother, engaging

stranger, eyes open

Less Preferred



stranger, eyes averted

stranger, eyes closed

…**sound** like caregivers.
…**smell** like caregivers.
…**move** like caregivers.
…**look** like caregivers.
…**interact** like caregivers.

Bushnell, Sai, & Mullin, 1989.
Simion, Valenza, Umiltà, & Barba, 1998.
Farroni, Csibra, Simion, & Johnson, 2002.
Batki, Baron-Cohen, et al, 2000.
Sai, 1990.
Sai, 2005.
Walton, Bower, & Bower, 1992.

Marcus AUTISM CENTER

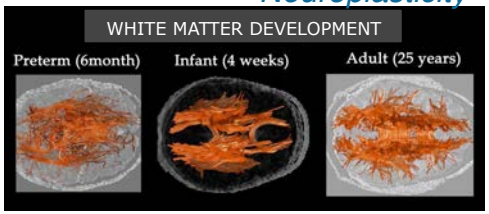
Universal Principle: the Platform for Development of Social Brain

Born to Socially Orient

MH Johnson PhD

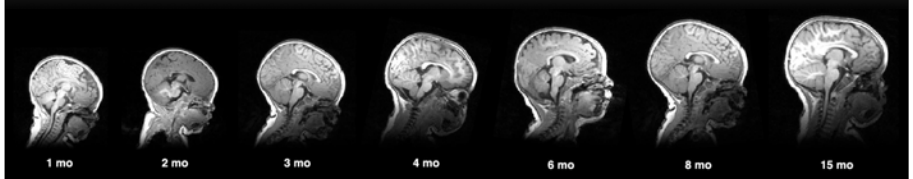
Reciprocal Social Interaction

Neuroplasticity



H-J Park PhD

Social Interaction is the Platform for Brain Development



Brain size doubles in the 1st year of a baby's life, synaptic density quadruples.

(Gilmore *et al*, 2007; Pfefferbaum *et al*, 1994; Huttenlocher, 1979; Petanjek et al, 2011; Shultz et al., 2018)

Social Visual Engagement…

…is strongly influenced by genetic variation.

(influencing millisecond timing of eye movements, with heritability of eye-looking ~0.90)

Constantino et al. (2017) *Nature*.

…reflects early-emerging differences in ASD.

(differences in ASD identifiable in the first 2-6 months after birth, and predictable of diagnosis and levels of disability at 24-36 months)

Jones & Klin. (2013) *Nature*.

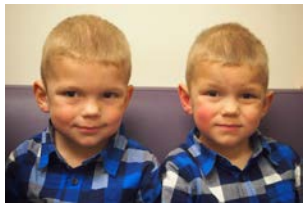
…is highly phylogenetically-conserved.

(similar patterns of early developmental change in looking observed in human infants and infant rhesus macaques, demonstrating evolutionary importance for early social development)

Klin et al. (2009) *Nature*; Wang et al. (2020) *Developmental Cognitive Neuroscience*

Evidence for biological relevance: Twins. How to link these quantifications of behavior to the genetic bases of autism?

Measuring the genetic structure of social visual engagement



250 toddlers:

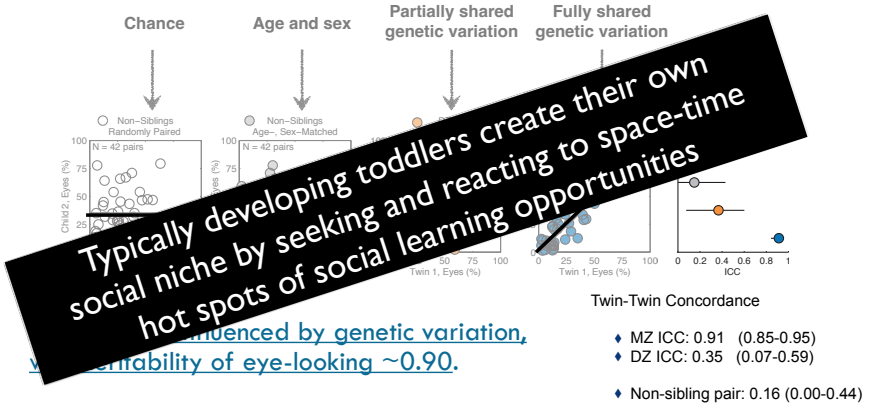
- **82 monozygotic** twins (41 MZ pairs)
- **84 dizygotic** twins (42 DZ pairs)
- **84** non-sibling comparison children (42 non-sib control pairs)
- age **21.3**(4.3) months
- non-sibs matched <1 day

Warren Jones PhD

John Constantino MD

Nature, 2017; 547(7663):340-344

Social Visual Engagement…



Twin-Twin Concordance

- MZ ICC: 0.91 (0.85-0.95)
- DZ ICC: 0.35 (0.07-0.59)
- Non-sibling pair: 0.16 (0.00-0.44)

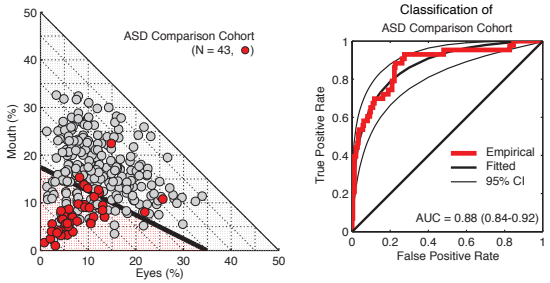
…influenced by genetic variation, …heritability of eye-looking ~0.90.

(influencing millisecond timing of eye movements, with heritability of eye-looking ~0.90)

Constantino et al. (2017) *Nature*.

Genetic influence exerts effects on a moment-by-moment basis.

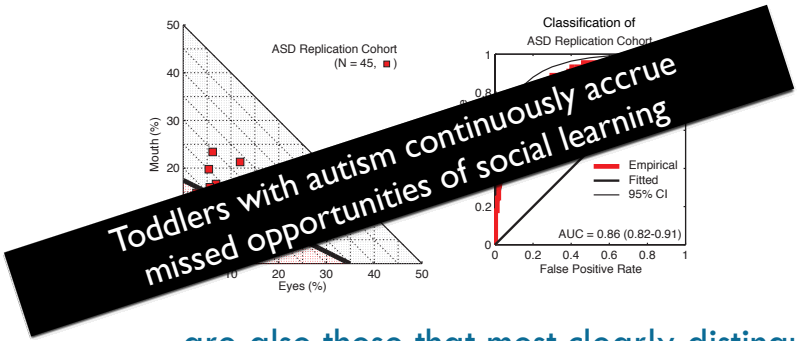
The markers of social visual engagement that are most highly heritable…



…are also those that most clearly distinguish typically-developing children from those with autism.

Constantino et al. (2017) *Nature*.

Replication Cohort



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Klin et al. (2009) *Nature*; Wang et al. (2020) *Developmental Cognitive Neuroscience*

Evidence for biological relevance: Human Infants
How early does it segregate children with autism?

Warren Jones PhD

2-6 month social visual engagement data predict diagnostic classification and level of social disability at ages 24 and 36 months

…reflects early-emerging differences in ASD.

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Klin et al. (2009) *Nature*; Wang et al. (2020) *Developmental Cognitive Neuroscience*

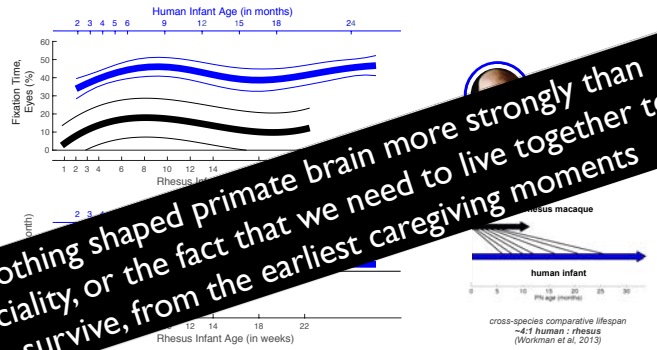
Marcus Autism Center

Evidence for biological relevance: Infant Monkeys

Jocelyne Bachevalier PhD

Sanchez PhD

Warren Jones PhD



Nothing shaped primate brain more strongly than sociality, or the fact that we need to live together to survive, from the earliest caregiving moments

…is highly phylogenetically-conserved.

(similar patterns of early developmental change in looking observed in human infants and infant rhesus macaques, demonstrating evolutionary importance for early social development)

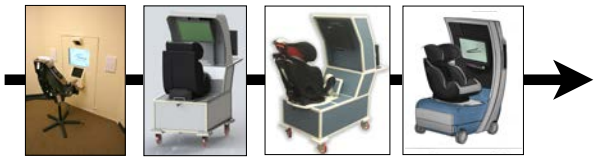
Wang et al. (2020) *Dev Cogn Neurosci*.

Can we leverage this biomarker to promote …

Greater Access to Early Diagnostic Services

The Tool

The original lab



The Prototype

The FDA: clearance in 2022 and 2023

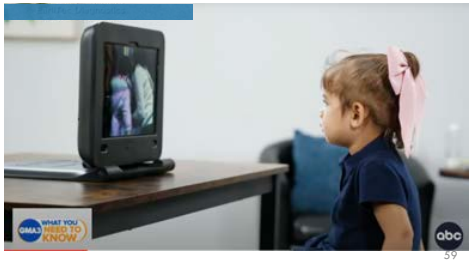
First meeting: October of 2014

Lab open to inspections and audits

Hundreds of thousands of code lines moved to tech industry standards

"Chain of Custody"

Repeatability & Reproducibility studies



The Clinical Trials

Methods

Warren Jones PhD

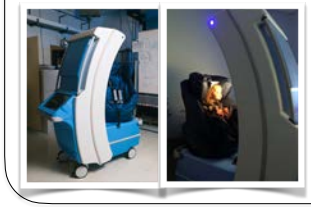
Cheryl Klaiman PhD

STARD

Standards for Reporting of Diagnostic Accuracy Studies

★ 12 minutes

★ 4-8 hours



VS Gold Standard Evaluations

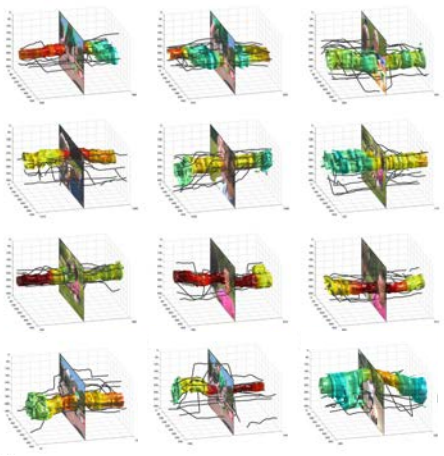
"Extraordinary Claims Require Extraordinary Evidence"

STARD: The Standards for Reporting of Diagnostic Accuracy

Simultaneous publications in JAMA & JAMA Network

Step 1: Derive Quantitative Indices for Early Identification of ASD

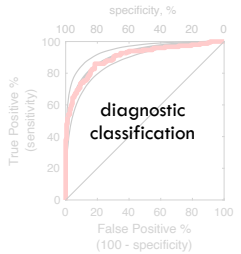
Methods



TD normative funnels =

ASD comparison scanpaths =

Gold Standard Evaluation

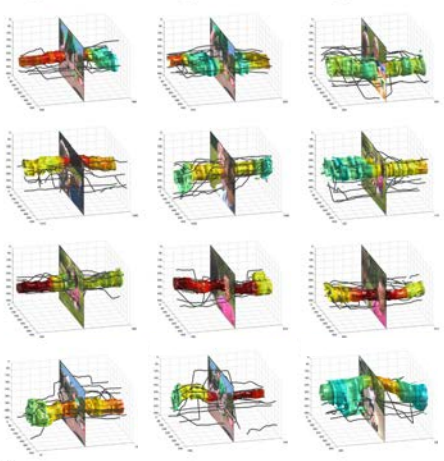


Mining 1000's of statistically significant moment-by-moment divergences from within minutes of naturalistic video viewing

Marcus Autism Center

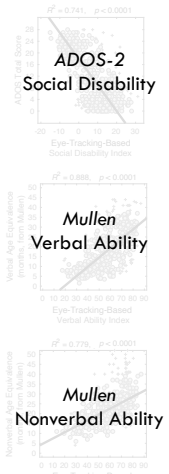
Step 2: Derive Quantitative Indices for Early Markers of Emerging Symptom Severity

Methods



TD normative funnels =

ASD comparison scanpaths =



Marcus Autism Center

3 Studies: Discovery, Replication, & Pivotal Trials

Studies

Goals: to test the accuracy of eye-tracking assays of social visual engagement in 16-30-month-old children to

1. accurately assess presence of ASD (
   best estimate using gold standard
2. accurately ass
   stand

>1,600 toddlers in 7 specialized centers and 1 community health center, 2 real-world replications, 3 independent cohorts, and 1 R&R study

oddlers (3 sites)

tudy; Marcus Autism Center (GA)

Replication Study; Forsyth Co. (GA) and WashU (MO)

Pivotal Trial: N=335 toddlers (6 sites)

- Multi-site, nationwide clinical trial (Seattle Children's, Cincinnati Children's, UCSF, Rush, SARRC, and Emory)

Feasibility Studies

Discovery & Replication: Participants, by Reference Standard Outcome Diagnosis

	Discovery Study (N = 719)		Replication Study (N = 370)	
Reference Standard Diagnosis	non-ASD	ASD	non-ASD	ASD
N	386	333	184	186
Age				
months: mean (SD)	21.7 (3.4)	23.1 (3.7)	22.7 (4.9)	28.1 (5.8)
percentiles [1st, 25th, 50th, 75th, 99th]	[15, 18, 23, 24, 30]	[16, 20, 24, 26, 30]	[16, 19, 21, 25, 36]	[17, 24, 28, 31, 43]
ADOS				
SA Score, mean (SD)	2.3 (2.3)	13.6 (4.1)	3.1 (2.6)	13.8 (4.4)
percentiles [1st, 25th, 50th, 75th, 99th]	[0, 1, 2, 3, 11]	[5, 10, 14, 17, 20]	[0, 1, 3, 5, 11]	[6, 10, 14, 17, 21]
RRB Score, mean (SD)	1.0 (0.9)	4.3 (1.8)	2.4 (1.6)	5.6 (1.4)
percentiles [1st, 25th, 50th, 75th, 99th]	[0, 0, 1, 2, 4]	[1, 3, 4, 6, 8]	[0, 1, 2, 4, 6]	[2, 5, 6, 7, 8]
Total Score, mean (SD)	3.3 (2.6)	17.9 (5.1)	5.5 (3.2)	19.4 (5.0)
percentiles [1st, 25th, 50th, 75th, 99th]	[0, 2, 3, 5, 12]	[8, 14, 18, 22, 27]	[0, 3, 5, 7, 13]	[8, 15, 20, 24, 28]
Mullen				
Verbal Age Equiv., mean (SD)	24.2 (5.6)	13.0 (6.2)	23.1 (8.0)	14.8 (7.7)
percentiles [1st, 25th, 50th, 75th, 99th]	[12, 20, 24, 28, 36]	[3, 8, 12, 16, 29]	[10, 16, 23, 28, 39]	[4, 10, 12, 18, 38]
Nonverbal Age Equiv., mean (SD)	24.8 (6.1)	19.0 (5.2)	27.3 (9.8)	20.7 (6.8)
percentiles [1st, 25th, 50th, 75th, 99th]	[15, 20, 24, 29, 40]	[7, 16, 19, 23, 32]	[13, 19, 25, 32, 48]	[9, 16, 20, 24, 42]

Jones et al. (JAMA Network Open 2023).

Pivotal Trial

Pivotal Trial enrolled 16-30-month-olds at 6 sites

COLLABORATING TRIAL TEAM:

- Chris Smith, SARRC, Phoenix, Arizona
- Shana Richardson, Emory University, Atlanta, Georgia
- Raphael Bernier, Mendy Minjarez, Seattle Children's, Seattle, Washington
- Ernest Pedapati, Cincinnati Children's, Cincinnati, Ohio
- Bennett Leventhal, Somer Bishop, Whitney Enns, UCSF, San Francisco, California
- Allison Wainer, Jenn Moriuchi, Rush, Chicago, Illinois

(https://clinicaltrials.gov/ct2/show/NCT03469986)

Jones et al. (2023) *JAMA*.

Pivotal Trial

Pivotal Trial: Participants, by Reference Standard Outcome Diagnosis

	N = 335	
Reference Standard Diagnosis	non-ASD	ASD
N	185	150
Age		
months: mean (SD)	23.4 (4.6)	
percentiles [1st, 25th, 50th, 75th, 99th]	[16, 19, 2	
ADOS		
SA Score, mean (SD)		
percentiles [1st, 25th, 50th, 75th, 99th]		
RRB Score, mean (SD)		
percentiles [1st, 25th, 50th, 75th, 99th]		, 6, 7, 8]
Total Score, mean (SD)		21.4 (4.1)
percentiles [1st, 25th, 50th, 75th, 99th]	, 10]	[10, 18, 22, 24, 28]
Mullen		
Verbal Age Equiv., mean (SD)	26.0 (8.2)	10.5 (5.3)
percentiles [1st, 25th, 50th, 75th, 99th]	[9, 20, 25, 32, 44]	[4, 7, 9, 13, 27]
Nonverbal Age Equiv., mean (SD)	27.4 (9.0)	17.3 (5.0)
percentiles [1st, 25th, 50th, 75th, 99th]	[14, 21, 26, 31, 50]	[8, 14, 17, 21, 29]
Other Diagnoses		
Presence of ≥1 (non-ASD) DD	162 (87.6%)	86 (57.3%)
Absence of ASD or DD diagnosis	23 (12.4%)	0 (0.0%)

Diagnostic composition of samples was typical of centers with complex cases of toddlers with autism and other neurodevelopment disabilities

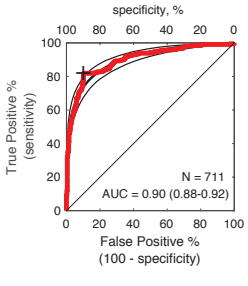
toddlers with non-ASD diagnosis, 162 (87.6%) had other, non-ASD developmental delays (DDs); only 23 (12.4%) had no diagnosis (i.e., were unaffected). Of the 150 toddlers with ASD, 86 (42.7%) had no developmental delays.

Jones et al. (JAMA 2023).

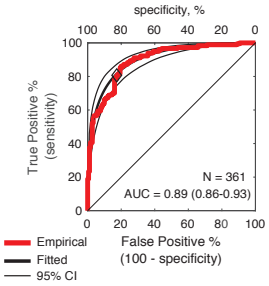
Results

Results: Presence of ASD - Diagnostic Accuracy

Discovery Study



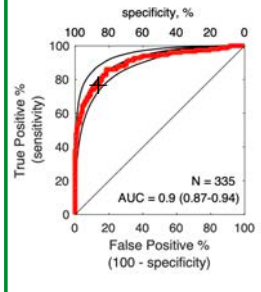
Replication Study



Empirical
Fitted
95% CI

	%	95% CI
Sensitivity	80.6	(74.1-85.7)
Specificity	82.3	(76.1-87.2)
PPV	81.9	(75.6-86.9)
NPV	81.0	(74.7-86.0)
Accuracy	81.4	(77.1-85.1)

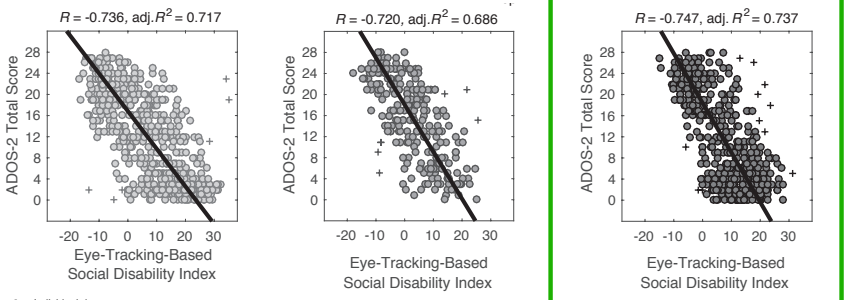
Multi-Site, Nationwide Clinical Trial



	%	95% CI
Sensitivity	78.0	(70.7-83.9)
Specificity	85.4	(79.5-89.8)
PPV	81.3	(74.0-86.8)
NPV	82.7	(76.7-87.5)
Accuracy	82.1	(77.6-85.8)

Results

Quantitative Indices for Assessing Severity: Social Disability (proxying ADOS-2)



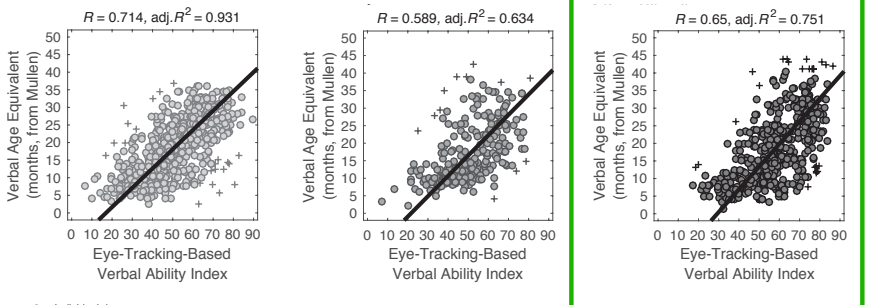
Discovery Study

Replication Study

Multi-Site, Nationwide Clinical Trial

Results

Quantitative Indices for Assessing Severity: Verbal Ability (Proxying Mullen)



Discovery Study

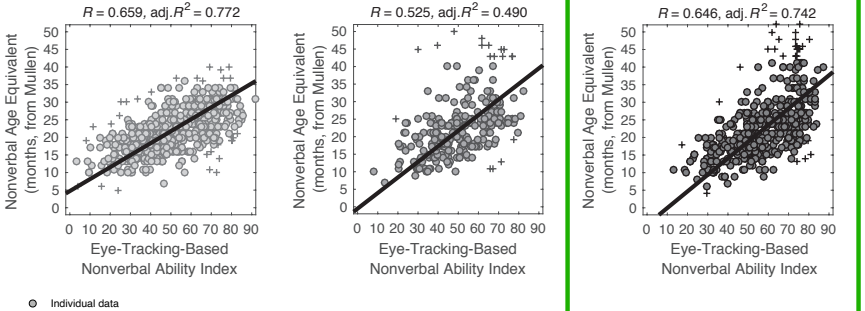
Replication Study

Multi-Site, Nationwide Clinical Trial

Note span of Y axis: eye-tracking metrics effectively proxy verbal function from 5-36 months.

Results

Quantitative Indices for Assessing Severity: Nonverbal Ability (Proxying Mullen)



Discovery Study

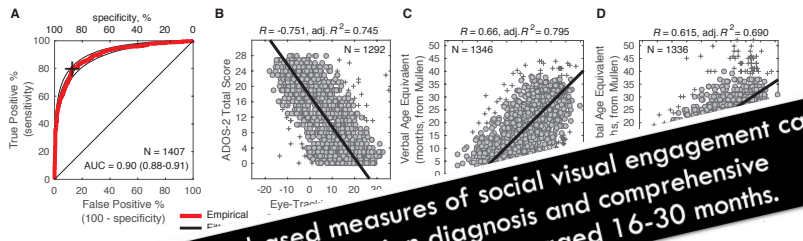
Replication Study

Multi-site, Nationwide Clinical Trial

Note span of Y axis: eye-tracking metrics effectively proxy nonverbal ability from 8-40 months.

Effective in Nationwide Clinical Trial: Successfully Proxying Diagnosis & Severity

✷ Pooled performance: se ~80%, ~sp 87%, ~74% of ADOS variance, ~79% of Mullen verbal variance, and ~70% of Mullen nonverbal variance.



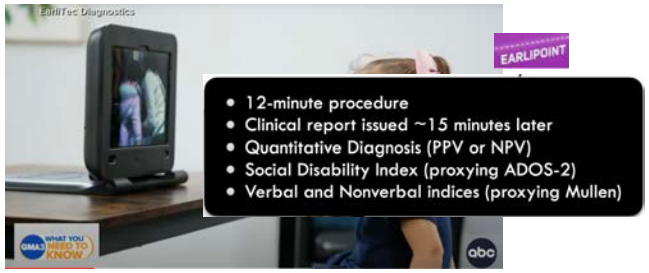
Objective eye-tracking-based measures of social visual engagement can effectively proxy expert clinician diagnosis and comprehensive evaluation of symptom severity in children aged 16-30 months.

Jones et al. (2023) *JAMA & JAMA Network Open.*

FDA clearance of tablet: July 2023

First children seen clinically: August 2023

The device



Relative to 6-10 hour of expert clinician evaluations

What is the EarliPoint-aided Evaluation of Toddlers?

The first FDA-cleared indication

FDA

EarliTec Diagnostics Inc.

The horizon for new indications

EarliTec Diagnostics Inc.

Population-based Screening
badly needed

- Vans at community pediatric practices
- Data collection integrated with pediatrician well-child visits
- 2 studies
  - screening at 9 months, children followed until 24 months
  - screening at 18 and 24 months

Other national clinical trials underway; and other functionalities

From 16-30 months to 7 years

Quantitative biomarkers for Treatment Response

PPV-NPV-based step-by-step clinical decision making

Clinical report writing aide

Quantitative indices for pivotal skills targeted in treatment

"Deep Phenotyping for large research networks

Imagine a world ….

To change the narrative of autism from one of disability to one of possibility and promise.

Thank you

Selected References

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Thank You

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- The National Institute of Mental Health
- The National Institute of Child Health and Human Development
- The JB Whitehead Foundation
- Autism Science Foundation

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