Meeting of the Interagency Autism Coordinating Committee

Wednesday, April 25, 2017

National Institutes of Health
31 Center Drive Building
31, C Wing, 6th Floor, Conference Room 6
Bethesda, MD 20892

Conference Call Access:
Phone: 800-857-9708
Access Code: 4617338

These slides do not reflect decisions of the IACC and are for discussion purposes only.

Meeting of the IACC

Morning Agenda

9:00 AM **Welcome, Introductions, Roll Call and Approval of Minutes**

Joshua Gordon, M.D., Ph.D.
Director, NIMH and Chair, IACC

Susan Daniels, Ph.D.
Director, OARC, NIMH and Executive Secretary, IACC

Meeting of the IACC

Morning Agenda – continued

9:10 **Update from Office of the National Autism Coordinator**

Thomas Novotny, M.D.
Deputy Assistant Secretary for Health and National Autism Coordinator
Department of Health and Human Services

9:15 **The Honorable Mike Lake, P.C., M.P.**
Member of Parliament for Edmonton-Wetaskiwin, Canada

Update from Office of the National Autism Coordinator

Thomas Novotny, M.D.
Deputy Assistant Secretary for Health and National Autism Coordinator
Department of Health and Human Services


@MikeLakeMP

"I've learned that people will forget what you said, people will forget what you did, but people will never forget how you made them feel."

Maya Angelou

@MikeLakeMP


To access this video, please visit https://www.facebook.com/MikeLakeMP/videos/1138205282876998/

“You can't live a perfect day without doing something for someone who will never be able to repay you.”

John Wooden

@MikeLakeMP


LIVE
To access this video, please visit https://www.youtube.com/watch?v=VofLfCGckC4

“To wear your heart on your sleeve isn't a very good plan; you should wear it inside, where it functions best.”

Margaret Thatcher

@MikeLakeMP


To access this video, please visit http://www.cnn.com/2012/09/28/health/new-york-autism-event/index.html

"If there is anything that a man can do well, I say let him do it. Give him a chance."

Abraham Lincoln

@MikeLakeMP

To access this video, please visit http://globalnews.ca/video/603450/bye-bye-birdie-star

“Everyone is a genius. But if you judge a fish on its ability to climb a tree, it will live its whole life believing it is stupid.”

Albert Einstein

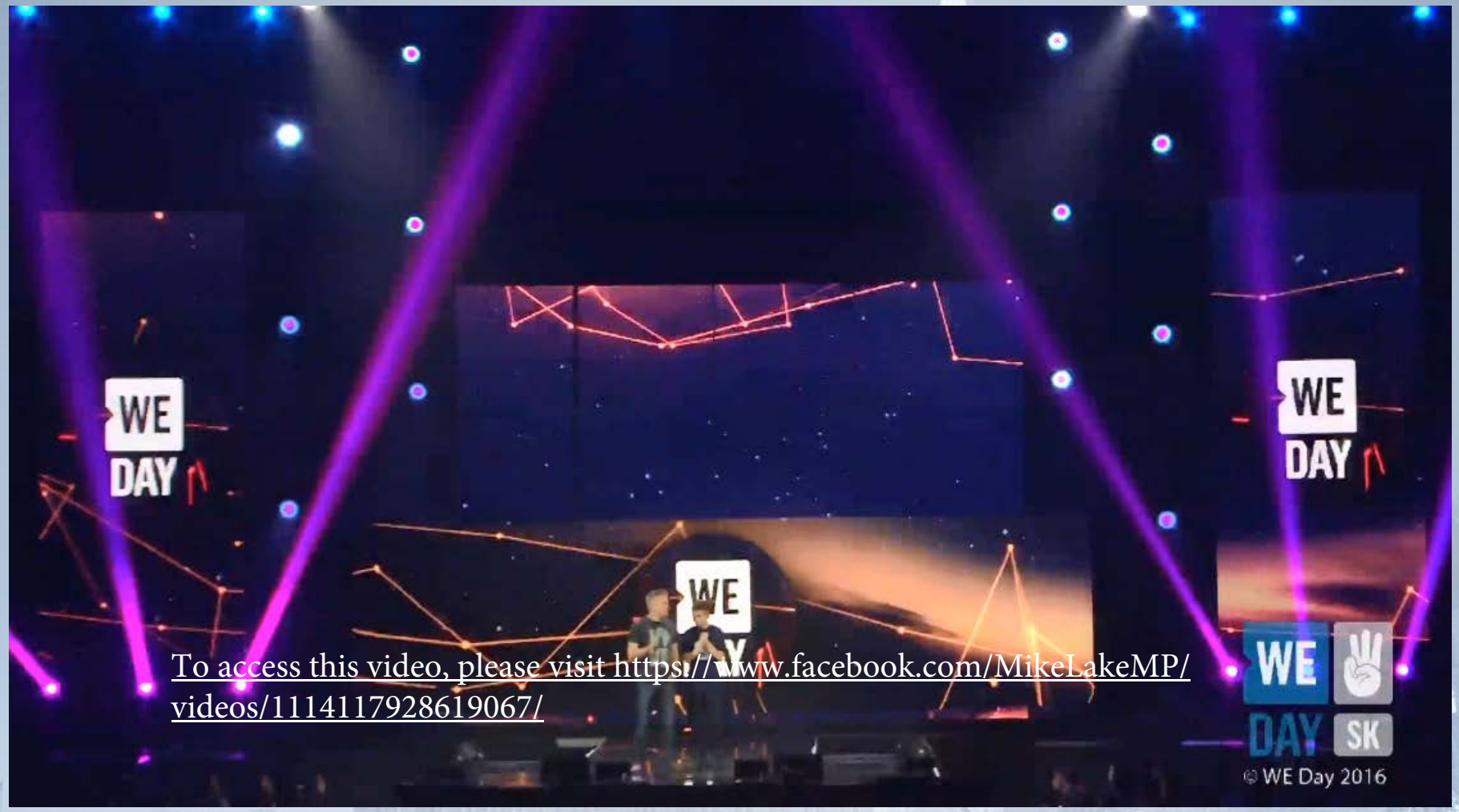
@MikeLakeMP


EDMONTON
To access this video, please visit http://www.ctvnews.ca/canada/canadians-with-autism-have-untapped-skills-when-it-comes-to-employment-1.2115018

"Life is a succession of lessons which must be lived to be understood."

Helen Keller

@MikeLakeMP



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"Things do not happen. Things are made to happen."

John F. Kennedy

@MikeLakeMP

"A small body of determined spirits fired by an unquenchable faith in their mission can alter the course of history."

Mahatma Gandhi

@MikeLakeMP


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Meeting of the IACC

Morning Agenda - continued

10:15 **Social Security Administration Disability Programs**

Melissa Spencer
Deputy Associate Commissioner, Office of Disability Policy Social Security Administration

10:30 **Morning Break**

Office of Retirement and Disability Policy

Office of Disability Policy (ODP)

Policy in Motion

Disability Benefits and Autism Spectrum Disorder

Securing today and tomorrow











Agenda

- Disability 101
- Disability Criteria for Autism Spectrum Disorders
- Application Process
- Demonstration Projects

What disability programs does the Social Security Administration administer?

The Social Security Administration (SSA) administers two programs that provide benefits based on disability:

The Social Security Disability Insurance (SSDI) program, authorized by Title II of the Social Security Act; and

The Supplemental Security Income (SSI) program, authorized by Title XVI of the Act

Social Security Disability Insurance (SSDI) Benefits – Title II

Date last insured: Must meet recent work and duration of work tests

Monthly benefit amount is based on average lifetime earnings

A **5-month waiting period** after disability benefits are awarded

Eligible for **Medicare after 2 years**

For more information: https://www.ssa.gov/pubs/EN-05-10029.pdf

Supplemental Security Income (SSI) Payments – Title XVI

Means-tested: To be eligible, must have limited income and resources

Monthly payments to:

Adults age 65 and older, blind, or disabled
Children (birth to attainment of age 18) blind or disabled

Eligible for **Medicaid**

For more information: www.socialsecurity.gov/ssi/text-eligibility-ussi.htm

Social Security's Definition of Disability

The general definition of disability under Title II and, for adults under Title XVI, is:

[The] **inability to engage in any substantial gainful activity** by reason of any medically determinable physical or mental impairment which can be expected to result in death or which has lasted or can be expected to last for a continuous period of not less than 12 months.

For children under Title XVI is:

[The child] has a medically determinable physical or mental impairment, which **results in marked and severe functional limitations**, and which can be expected to result in death or which has lasted or can be expected to last for a continuous period of not less than 12 months.

How do we determine if someone qualifies for disability?

Sequential Evaluation

Step 1 – Is the individual working ("substantial gainful activity")?

SSA defines SGA according to monthly earnings: 2017 SGA amount is $1,170

Step 2 – Is the impairment severe?

Severe impairment means any impairment or combination of impairments which significantly limits an individual's physical or mental ability to do basic work activities

Step 3 – Does the impairment meet or medically equal a listing?

Sequential Evaluation

Step 4 – Can the individual still do <u>past relevant work</u>?

We determine whether the individual's residual functional capacity – which is the most we expect an individual can do despite the impairment – prevents the individual from performing any past relevant work

Step 5 – Considering age, education, and work experience, can the individual make an adjustment to <u>other work</u>?

We determine whether an individual can do OTHER work that exists in significant numbers in the national economy

Establishing the Medically Determinable Impairment (MDI)

An MDI must result from anatomical, physiological, or psychological abnormalities that can be shown by medically acceptable clinical and laboratory diagnostic techniques

To establish an MDI, we require objective medical evidence from an acceptable medical source

We do not use an individual's statement of symptoms, a diagnosis, or a medical opinion to establish the existence of the MDI

Determining Impairment Severity for Autism Spectrum Disorder

Psychiatric Review Technique (PRT)

PRT involves using a five-point rating scale to rate the degree of limitation an individual has using the four areas of mental functioning (the “Paragraph B” criteria)

Paragraph B criteria:

- Understand, remember, or apply information
- Interact with others
- Concentrate, persist, or maintain pace
- Adapt or manage oneself

Determining Impairment Severity for Autism Spectrum Disorder

PRT and Five-Point Rating Scale

No limitation – Able to function

Mild limitation – Functioning is slightly limited

Moderate limitation – Functioning is fair

Marked limitation – Functioning is seriously limited

Extreme limitation – Not able to function

Step 3 – Listing Criteria

12.10 and **112.10** *Autism spectrum disorder*

Paragraph A – Medical criteria

Paragraph B – Functional criteria

Listings 12.10 and 112.10

Paragraph A – Medical Criteria

A. Medical documentation of both of the following:

1. Qualitative deficits in verbal communication, nonverbal communication, and social interaction

2. Significantly restricted, repetitive patterns of behavior, interests, or activities

Listings 12.10 and 112.10
Paragraph B – Functional Criteria

B. Extreme limitation of one, or marked limitation of two, of the following areas of mental functioning:

1. Understand, remember, or apply information
2. Interact with others
3. Concentrate, persist, or maintain pace
4. Adapt or manage oneself

How does someone apply for benefits through SSA?

Adults can complete the application process online at www.socialsecurity.gov, or call our toll-free number, 1-800-772-1213, to make an appointment at a local SSA office.

The application process for children must be completed in-person at a local SSA office.

When you apply for either SSDI or SSI, we will collect medical and other information from you and make a decision about whether or not you meet Social Security's definition of disability.

What information does SSA need from an applicant?

- ❑ Social Security number
- ❑ Birth or baptismal certificate
- ❑ Names, addresses and phone numbers of the doctors, caseworkers, hospitals and clinics that took care of the individual, and dates of visits
- ❑ Names and dosage of all the medicine he or she takes
- ❑ Medical records that the individual already has in his/her possession
- ❑ Laboratory and test results
- ❑ A summary of where he or she worked and the kind of work performed
- ❑ A copy of his or her most recent W-2 Form (Wage and Tax Statement) or, if self-employed, federal tax returns for the past year

Supported Employment Demonstration (SED)

Background	**Purpose** • SSA will evaluate whether offering evidence-based packages of integrated vocational, medical, and mental health services to recently denied disability applicants could reduce the demand for SSA disability benefits
Intervention Design	**Participants** • Individuals aged 18-50 who express a desire to work and who have been recently denied disability benefits (DI or SSI) while alleging a mental illness **Randomized Experiment** • Coordinating with 30 community health centers across the country, SED will enroll and randomly assign 3,000 participants into one of three arms: o *Full Treatment Arm*: Participants receive Individual Placement and Support (IPS) services, a nurse care coordinator, systematic medication management, and assistance with cost sharing for medications and behavioral-health and work related expenses o *Basic Treatment Arm*: Participants will receive IPS services and assistance with behavioral health and work-related expenses o *Control Arm*: Participants will have access to all behavioral health or employment – related services available at the community health center and will receive a local Community Resources information book

Supported Employment Demonstration (SED) Continued

Project Activities	**Current Project Activities** • Final site selections; testing of survey tools; awaiting OMB clearance (FY2017) • Enrollment begins September 1, 2017; 36 months of services to enrollees (FY2017-2020)
Budget	• SSA: $72.5M over 6 years (Section 1110)

Promoting Readiness of Minors in SSI (PROMISE)

Background	**Purpose** • Promote positive outcomes for youth who receive SSI and their families through improved provision and coordination of employment and education services; long-term reduction in youth's reliance on SSI **Inter-agency Initiative** • Department of Education (ED) awarded 6 grants in September 2013 to 5 individual states—Arkansas, California, Maryland, New York, Wisconsin—and one consortium of 6 states (Arizona, Colorado, Montana, North Dakota, South Dakota, Utah); the 6 grantees designed and are implementing separate Model Demonstration Projects **SSA** • Responsible for the national evaluation; awarded a contract to Mathematica Policy Research in late FY13 • Random assignment design; minimum sample of 2,000 youth per project—1,000 treatment and 1,000 control
Intervention Design	**Unique Model in Each State/Consortium with Common Elements** • Formal partnerships expected between state agencies; Services must include case management, benefits counseling, career and work-based learning experiences, and parent training and information **Eligibility** • Non-institutionalized SSI recipients ages 14-16 and their families
Project Activities	**Current Status** • Enrollment ended April 2016 • Services provided (ED) through September 2018

Promoting Opportunity Demonstration (POD)

Background

Purpose

- Section 823 of the Bipartisan Budget Act of 2015 requires SSA to conduct a five-year (2017 to 2021) demonstration to test a benefit offset for Social Security Disability Insurance (DI) beneficiaries, including a simplification of work incentives, intended to promote employment.

Section 823 of the Bipartisan Budget Act of 2015

- Benefits reduced $1 for every $2 earned greater than the beneficiary's impairment-related work expenses (IRWE) or a threshold determined by SSA but no greater than SGA
- Entitlement to benefits may terminate due to work if benefits are reduced to zero
- The Trial Work Period and Extended Period of Eligibility do not apply
- Continued Medicare eligibility for 93 months after termination, if the impairment continues

Intervention Design

Randomized Experiment

- Recruit, enroll, and randomly assign (starting October 2017) 15,000 volunteers into three groups (approximately 5,000 per group) – control group continues under current law rules, one treatment group receives the benefit offset and no termination of entitlement in full offset (benefits are zero), and a second treatment group receives the benefit offset with termination of entitlement after 12 consecutive months in full offset
- Each month, beneficiaries must report earnings and IRWE for the prior month to offset the benefit paid in the following month.
- The standard POD monthly offset threshold is the TWP-level of SGA ($840 in 2017)
- All participants volunteer and provide written informed consent

Eligibility

- DI Worker beneficiaries at least age 20 and under 62 throughout the project

Benefit Offset National Demonstration (BOND)

Background	**Purpose** • The Ticket to Work and Work Incentives Improvement Act of 1999 directed SSA to conduct a demonstration projects evaluating the effects of a $1 for $2 withholding of Social Security Disability Insurance (DI) payments for earnings over a level specified by the Commissioner • Designed to test whether a benefit offset will encourage return to work • Awarded the implementation and evaluation contract to Abt Associates (13 subcontractors) in December 2009
Intervention Design	**Two Stages, Randomized Experiment** • Stage 1: Non-volunteers assigned to two groups: o Treatment 1: offset for a five-year period; or o Control 1: no offset • Stage 2: Volunteers assigned to three groups: o Treatment 21: offset for a five-year period; or o Treatment 22: offset for a five-year period with Enhanced Work Incentives Counseling; or o Control 2: no offset **Eligibility** • The BOND sites are in operation in the following states: Alabama, Arizona and southern California, Colorado and Wyoming, Washington, D.C. metropolitan area, Greater Detroit, Greater Houston, Northern New England, Southern Florida, Western New York, and Wisconsin. • Beneficiaries must be between 21 and 59 at the time of enrollment

Benefit Offset National Demonstration (BOND) Continued

Project Activities	**Current Status**
	• Enrollment closed in September 2012
	  o Stage 1: 968,145 beneficiaries
	  o Stage 2: 12,744 beneficiaries
	• Ongoing treatment services such as work incentives counseling (WIC) and enhanced work incentives counseling (EWIC), and helping beneficiaries use the offset will continue until September 2017. The contract ends December 2018.
	Timeline/Reports
	• Multiple reports released on SSA demonstration page
	• Participation, Process and Impact report drafts due April - June 2017
	• Final report draft due October 2017

Budget	• $128M over 9 years (Section 234) • Remaining: FY2017: $6.7M; FY2018: $5.6M

38

my Social Security

Create a *my* Social Security account to verify your earnings or see an estimate of future benefits while still working and manage your monthly benefits once you begin receiving payments.

Step 1: Visit www.socialsecurity.gov/myaccount and select *my* Social Security

Step 2: Select “Create an Account”

IACC
INTERAGENCY AUTISM
COORDINATING COMMITTEE

Break

Meeting of the IACC

Morning Agenda - continued

10:40 **Report from Advisory Committee on Increasing Competitive Integrated Employment for Individuals with Disabilities**

Scott Michael Robertson, Ph.D.
Andrew Arias
Office of Disability Employment Policy
U.S. Department of Labor

DOL and ODEP Logos

Driving Change,
Creating Opportunity

Recommendations from the Advisory Committee on Increasing Competitive Integrated Employment for Individuals with Disabilities

Interagency Autism Coordinating Committee Public Meeting
NIH Main Campus, April 26, 2017

Scott Michael Robertson, PhD
Policy Advisor, Youth Policy Team

Andy Arias
Policy Advisor, Workforce Systems Policy Team

Office of Disability Employment Policy, U.S. Department of Labor

ODEP's Core Mission as Federal Agency Guides Our Work

The Office of Disability Employment Policy (ODEP) is the only non-regulatory federal agency that promotes policies and coordinates with employers and all levels of government to increase workplace success for people with disabilities.

- ODEP's Website: www.dol.gov/odep/
- Campaign for Disability Employment: www.whatcanyoudocampaign.org/
- National Disability Employment Awareness Month (annually in October): www.dol.gov/odep/topics/ndeam/

Autism: Increasing Access to Competitive, Integrated Employment

- Substantial unemployment and underemployment among autistic adults across life course
- Less access to work-based learning and career exploration and development opportunities for autistic youth
- Workplace self-disclosure barriers for autistic people
  - Myths and stigma widespread
  - Self-advocacy and self-determination needed for disclosing differences, such as with body language and eye contact
- Improvements in career pathways and workforce development for autistic youth and adults needed
- Gifts and talents, including focused interests, to drive gainful employment opportunities
- Increased access to coaching, peer mentoring, etc.

Workforce Innovation and Opportunity Act Improves Employment Access

- Workforce Innovation and Opportunity Act (WIOA) signed into law on July 22, 2014
- Strong emphasis on:
  - Full access to competitive integrated employment for youth and adults with disabilities
  - Access to customized employment and supported employment for people with significant disabilities
- Prioritization on:
  - Alignment and coordination among workforce development and other service systems
  - Employer engagement to tap skills of youth and adults to benefit businesses, including through career pathways

WIOA Promotes Greater Employment Access for Youth with Disabilities

- Pre-Employment Transition Services for students with disabilities (Pre-ETS) under WIOA
- Students with disabilities aged 14-21
- Disability eligibility under Individuals with Disabilities Education Act (IDEA) or Rehabilitation Act Section 504
- 4 Core Areas of Required Services:
  - Job exploration counseling and work-based learning experiences, including internships
  - Counseling on postsecondary education and training opportunities, including comprehensive transition programs
  - Instruction in self-advocacy skill development
  - Workplace readiness training to develop social skills and independent living skills

WIOA Section 511 Improves Access to Employment for Youth with Disabilities

- WIOA Section 511 prioritizing competitive, integrated employment for youth aged under 24
- Restrictions on placements in settings paying less than federal minimum wage through 14C certificates
- Before any consideration of such placements, 3 criteria must be met in full by the individual:
  1. Received pre-employment transition services (pre-ETS)
  2. Applied for vocational rehabilitation (VR) services
     - Been deemed ineligible for services *or*
     - Had case closure without successful progress toward employment outcome
  3. Received career counseling and information and referral to other programs offering employment-related services

WIOA Supports Equal Opportunity Access and Non-Discrimination

- Section 188 ensuring equal opportunity and non-discrimination in all WIOA programs and services
- Non-discrimination protection for race, color, religion, sex, national origin, **disability**, age, and political affiliation/belief
- Read guidance on implementing Section 188 in LEAD Center's policy brief on disability perspective of final rule: www.leadcenter.org/system/files/resource/downloadable_version/Sec_188_Final%20Rule_Summary_Dec_2016.pdf

WIOA charged Advisory Committee with Developing Recommendations

- WIOA Section 461: modification of Rehabilitation Act Section 609
  - Advisory Committee on Increasing Competitive, Integrated Employment for Individuals with Disabilities (the Committee)
  - ODEP coordination of Committee's activities
- 10 public meetings between January 22, 2015 and August 29, 2016 (face-to-face and webinar)
- Final report of Committee released to Congress, Secretary of Labor, and public on Sept. 9, 2016 www.dol.gov/odep/topics/pdf/ACICIEID_Final_Report_9-8-16.pdf

Advisory Committee's Final Report Outlines Six Recommendations

1. Increasing Competitive Integrated Employment Will Require Capacity Building
2. Capacity Building for Youth
3. Capacity Building through Changes in the Use and Oversight of 14(c) Certificates
4. Capacity Building in the Marketplace
5. Capacity Building in Specific Federal Agencies
6. Increasing Competitive Integrated Employment in the AbilityOne® Program

1. Overall Capacity Building

In order to build more systemic capacity for CIE, there needs to be:

1. Guidance, policies, and strategies to prioritize federal funding for CIE

2. Data collection and analysis requirements for recipients of federal funding based on a common definition of CIE and outcomes

3. Funding and initiatives to help agencies build CIE capacity, develop national standards of professional competence, and train professionals skilled in facilitating CIE

4. A federal interagency task force focused on policies to expand capacity of CIE and advance economic self-sufficiency

2. Capacity Building for Youth

For youth to effectively transition to adult employment there needs to be:

1. Early work experiences
2. Family involvement and support
3. Professional development and training
4. Systems integration for seamless transition
5. Available and transferable assistive technology

3. Capacity Building through Changes in the Use and Oversight of 14(c) Certificates

Subminimum wages paid under certificates allowable under Section 14(c) of the FLSA inhibit participation in CIE. To address this, the Committee recommends that:

1. Congress amend the FLSA to allow for a multi-year, well-planned phase out of Section 14(c)

2. The Wage and Hour Division of the U.S. Department of Labor engage in stronger oversight of the current use of 14(c) certificates

3. The federal government assists states with building capacity of service systems to provide CIE services as alternatives to those provided under programs using a 14(c) certificate

4. Building Capacity in the Marketplace

Increased business and employer engagement will be necessary to increase CIE and will require:

1. Increased and more effective communication and outreach to businesses
2. Specific business-oriented professional development for employment services personnel
3. Incentives to create work experiences as preludes to employment
4. Expansion of available benefits counseling and financial coaching

4. Building Capacity in the Marketplace (Cont.)

Increased business and employer engagement will be necessary to increase CIE and will require:

5. More accessible transportation

6. Hiring initiatives in high-growth industries, particularly healthcare

7. Additional outreach to federal contractors regarding the Office of Federal Contract Compliance Programs (OFCCP) Section 503 regulations which establish disability hiring goals

8. Revisions to federal tax incentives and credits available to employers who hire people with disabilities

5. Capacity Building in Specific Federal Agencies

Increasing CIE will require partnerships and complementary actions among multiple federal agencies, including these activities:

1. Establishing a cross-agency working group to provide policy guidance and technical assistance on integrated day and wraparound services that complement and maximize CIE and that advance the socioeconomic status and security of people with disabilities

5. Capacity Building in Specific Federal Agencies (Cont.)

Increasing CIE will require partnerships and complementary actions among multiple federal agencies, including these activities:

2. Demonstrating how the waiver of certain requirements in the Ticket to Work program will enable youth receiving Supplemental Security Income/ Social Security Disability Insurance (SSI/SSDI) to access services across systems that lead to CIE and

3. Developing a policy reform initiative designed to increase the number of SSI/SSDI beneficiaries in CIE and who are self-sufficient

6. Increasing Competitive Integrated Employment in the AbilityOne® Program

Reforming the AbilityOne® Program so that it can create CIE opportunities on a broad scale will require:

1. Amending the Javits-Wagner-O'Day Act (JWOD) to fully align the Act with modern federal disability law and policy goals by reforming the criteria for contract procurement selection and for program eligibility

2. Researching the current use of AbilityOne to identify how the program is serving the target population and to determine steps for improving its ability to create CIE opportunities

3. Evaluating the implementation and impact of AbilityOne reforms

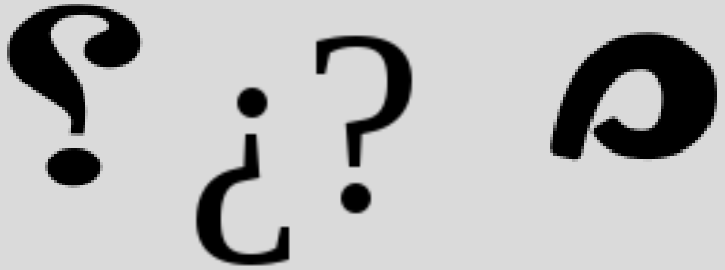
Sharing Conclusion of Final Report

“The work of the Committee, and the formation of its recommendations, was intended to increase opportunities for CIE for individuals with I/DD or other significant disabilities.”

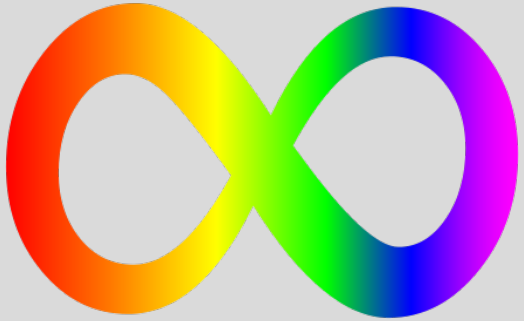
“Ensuring that CIE is the first option for people with I/DD or other significant disabilities will increase their employment participation rate and lead to a significant reduction in segregated work and non-work programs and in the use of Section 14(c) certificates for paying subminimum wages.”

“CIE will create a critical pathway to better economic future and increased economic self-sufficiency for youth and adults with disabilities.”

Q&A: Audience Members Ask Questions



Question mark shapes
from different languages



Multi-colored Infinity Symbol:
Autism and Neurodiversity

My email address: robertson.scott.m@dol.gov

ODEP's website: http://www.dol.gov/odep

Meeting of the IACC

Morning Agenda - continued

11:05 **Developing Services to Enhance Social Functioning in Adults with Autism, Spectrum Disorder**

Edward Brodkin, M.D.
Associate Professor of Psychiatry
Perelman School of Medicine,
University of Pennsylvania

Developing Services to Enhance Social Functioning in Adults with Autism Spectrum Disorder

EDWARD S. ("TED") BRODKIN, M.D.

Director, Adult Autism Spectrum Program, Penn Medicine
Associate Professor of Psychiatry
Perelman School of Medicine at the University of Pennsylvania

INTERAGENCY AUTISM COORDINATING COMMITTEE (IACC) MEETING

APRIL 26, 2017

Defining Symptom Domains of Autism Spectrum Disorder (ASD)

- Social interaction / Social communication
  - Social-emotional reciprocity
  - Nonverbal social communication
  - Developing, maintaining, and understanding relationships
- Restricted, repetitive, stereotyped patterns of interests or behaviors

The Need for Increasing Focus on Treatment and Services for Adults with ASD

- Approximately 500,000 – 600,000 adolescents with ASD will enter adulthood in the next decade in the USA

Challenges of Transition to Adulthood

- **Typical Challenges**:
  - Completing secondary or post-secondary education
  - Transitioning from educational setting to work setting
  - Developing social and communication skills necessary for adult life
  - Engaging with peers and the community
  - Developing independence / ability to function once one's parents become elderly or pass away
  - Difficulties with **social functioning** heighten all of these challenges.
  - Lack of evidence-based treatment programs to improve social functioning in adults with ASD

Social Outcomes in Adults with ASD

TABLE 4 Social Relationships

Rating	Friends/Acquaintances[a] (n = 59[b])	n (%)
0	One or more friend of approximately same age	5 (9)
1	One or more friend but restricted range of interests	9 (15)
2	No specific friendships but seeks contact with others in group situations	8 (14)
3	Never any peer relationships involving selectivity/sharing	37 (63)
	Close relationships[a] (n = 60)	
0	Close reciprocal relationship(s) (e.g., sexual relationship/marriage) past or present	4 (7)
1	Some reciprocal relationships but short duration and/or reduced sharing of activities	6 (10)
2	Only ever very brief relationships, involving minimal sharing of activities	4 (7)
3	No reciprocal relationships lasting >1 month or never had relationship	46 (77)

Note: [a]Friends are characterized as individuals seen for outings, visits outside the home but not necessarily involving emotional intimacy/sharing of feelings. Close relationships are characterized as involving close personal contacts (including sexual); sharing of feelings and activities.
[b]One informant could not report on this area.

From Howlin et al 2013 Social outcomes in mid- to later adulthood among individuals diagnosed with autism and average nonverbal IQ as children. *Journal of the American Academy of Child and Adolescent Psychiatry* 52:572-581

Residential Outcomes in Adults with ASD

TABLE 2 Residential Status (N = 60)

Rating	Where Living[a]	n (%)
0	Independently	8 (13)
1	Semi-sheltered accommodation (n = 5) or with parents but high degree of autonomy (n = 3)	8 (13)
2	At home, limited autonomy	10 (17)
	Residential home, limited autonomy	12 (20)
3	Specialist autistic placement or another placement with little/no autonomy	20 (33)
	Secure hospital care	2 (3)

Note: [a]All individuals in residential care had been there since early adulthood (age 18–21).

From Howlin et al 2013 Social outcomes in mid- to later adulthood among individuals diagnosed with autism and average nonverbal IQ as children. *Journal of the American Academy of Child and Adolescent Psychiatry* 52:572-581

Employment Outcomes in Adults with ASD

TABLE 3 Employment Status

Highest Occupation	Job Type (N = 60)	n (%)
Professional or highly skilled	Computer programmer (construction design); engineer (nuclear research)	2 (3)
Nonmanual skilled	Project manager × 2 (civil service; telecom); artist (self-employed); accounts clerk (× 2); town planner; civil servant	7 (12)
Manual skilled	Electronics work	1 (2)
Partly skilled	Postal workers (× 2)	2 (3)
Unskilled and untrained	Postal work (family firm); McDonald's; sales assistant; cleaning/sorting in theatrical costumiers; factory assembly/packing work	5 (8)
Ph.D. student/voluntary lobbying work		1(2)
Sheltered/voluntary employment	Basic industrial work/cleaning × 2; care-home/charity shop × 4; railway guard; kitchen/ gardening work × 2	9 (15)
Never worked/long-term unemployed		33 (55)

From Howlin et al 2013 Social outcomes in mid- to later adulthood among individuals diagnosed with autism and average nonverbal IQ as children. *Journal of the American Academy of Child and Adolescent Psychiatry* 52:572-581

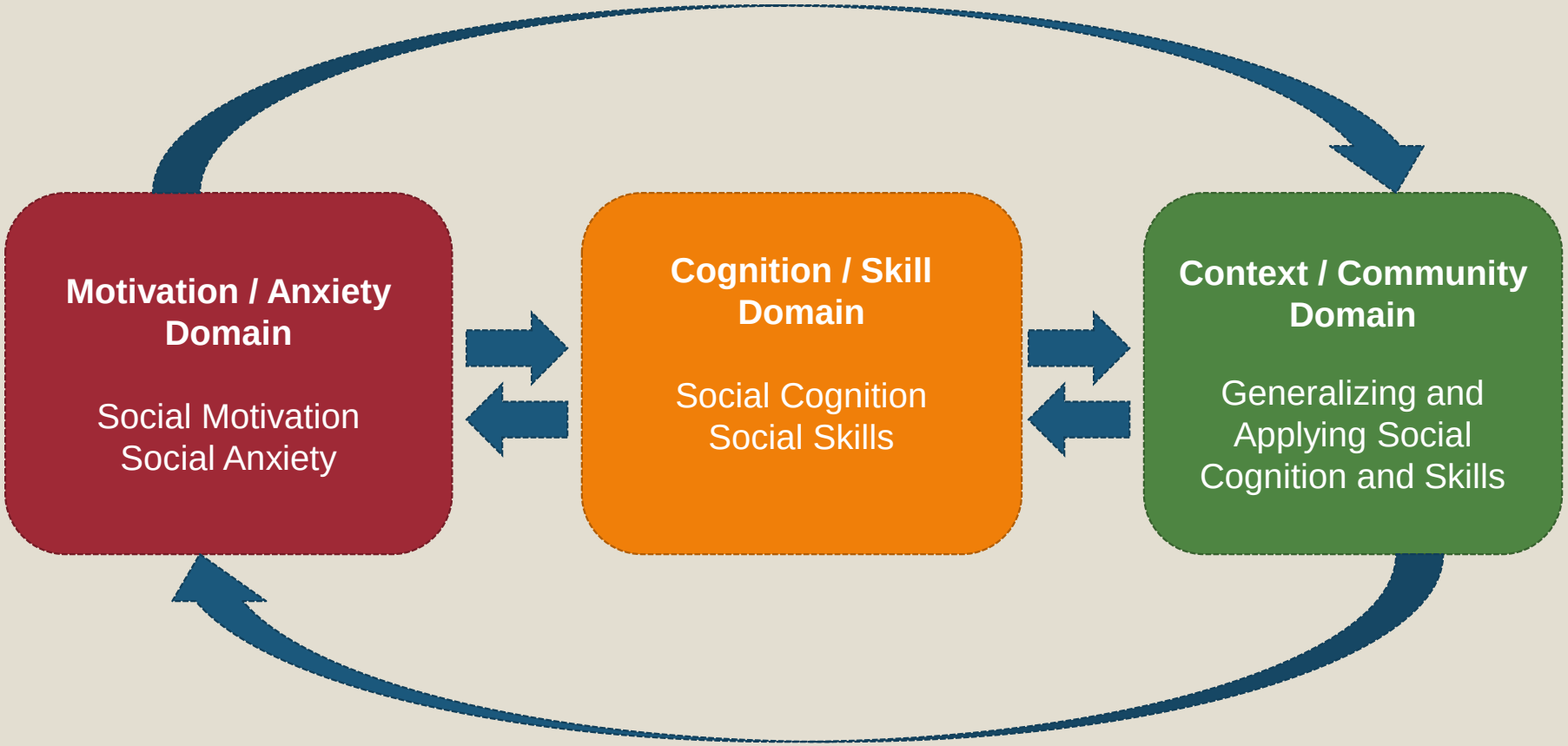
Importance of Social Functioning

- Social Functioning: ability to navigate the social world in real-world settings, including home, school, work, and community

- Difficulties with social functioning have been cited as one of the main barriers to employment, independence, and overall functioning in adults with ASD.

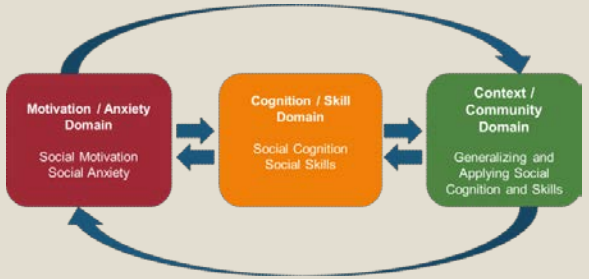
- Social Functioning has many components

Domains Essential for Social Functioning



TUNE In: Training to Understand and Navigate Emotions and Interactions

- NIMH R34MH104407, Brodkin, PI
- Study Period: August 2014 to August 2017
- Objective
  - To develop and pilot **a new treatment program** to improve **social functioning** in **adults** with ASD
- Strategy
  - Design a treatment program that addresses the many components of social functioning
  - A focus on the *fundamentals* of social functioning
    - Ability to tune into one's own state and into others
    - Ability to understand and navigate emotions
    - Ability to understand and navigate conversation
    - Generalize these skills to a community / work setting



- Tactics
  - The treatment program incorporates a variety of therapeutic "tools" to address social functioning (an eclectic treatment program)
  - Integration of cognitive, behavioral, and mindfulness-based approaches

Outline of TUNE In

- Determination of Eligibility
- Pre-Treatment Assessments
- Component 1—Social Motivation/Anxiety
  - 5 weekly individual sessions: Addressing goals / motivation, Cognitive Coaching, Exposure, Mindfulness
- Component 2—Social Cognition/Skill
  - 8 weekly group sessions: Group-based Social Cognition and Interaction Training for Individuals with ASD, Video Modeling of Social Skills
- Component 3—Generalization to Community
  - 4 weekly sessions: Participation in a Volunteer Work Team
- Post-Treatment Assessments

Study Eligibility, Setting, & Compensation

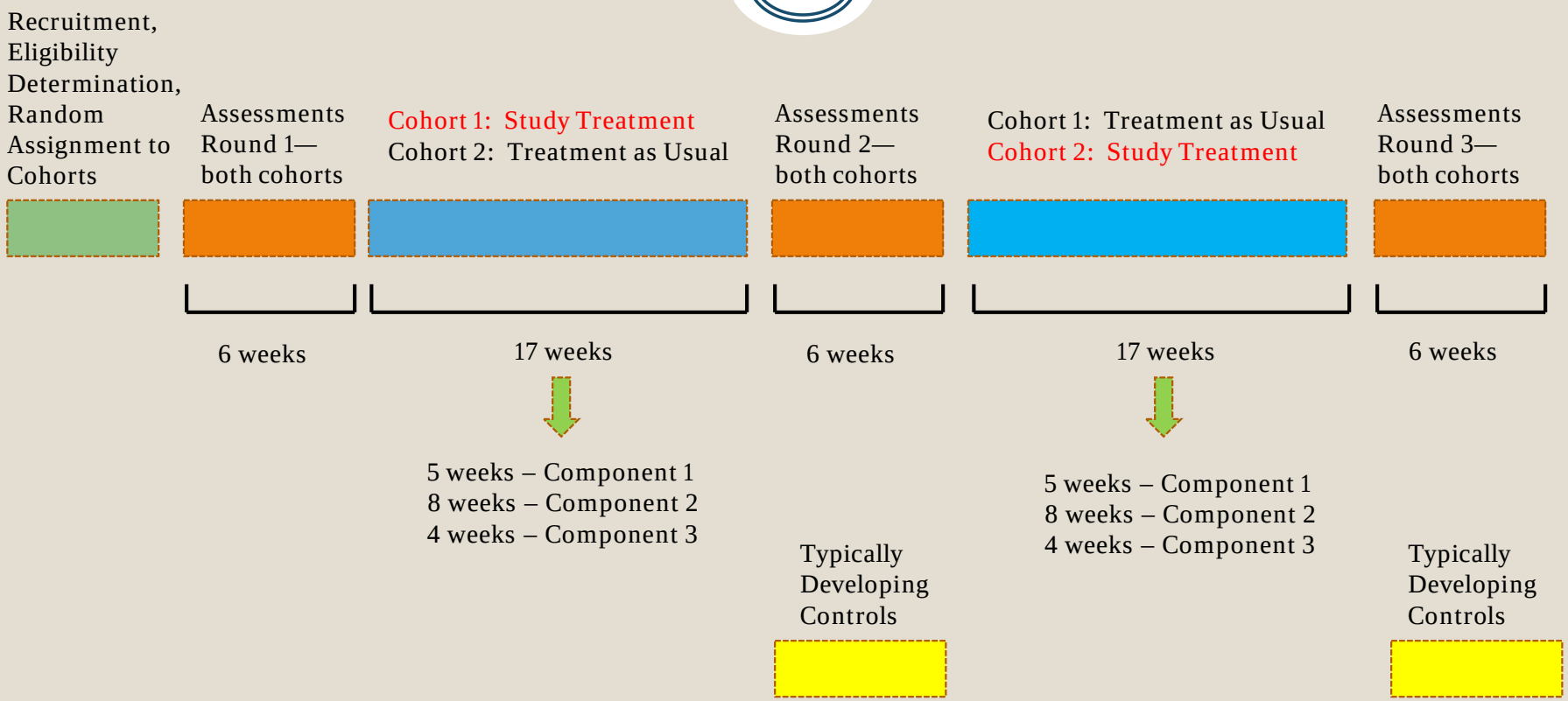
- Eligibility
  - Inclusion criteria: Adults age **18 years or older** with a diagnosis of autism spectrum disorder (**ASD**) who can attend **weekly sessions** (1-2 hours each) for a ~5 month period
  - Exclusion criteria: intellectual disability, current psychotic symptoms, current severe mood symptoms, current severe substance use disorder, recent suicidal or aggressive behaviors
- Setting
  - Perelman School of Medicine at the University of Pennsylvania and the Center for Autism Research at the Children's Hospital of Philadelphia

Participants

Demographics Summary

	N	Males	Females	White	African-American	Asian-American	Mean Age (years)	SD Age (years)
Cohort 1	**7**	**7**	**0**	**6**	**1**	**0**	**27.9**	**7.4**
Cohort 2	**13**	**11**	**2**	**13**	**0**	**0**	**27.8**	**8.9**
TOTAL	**20**	**18**	**2**	**19**	**1**	**0**		

Study Design / Timeline



Pre/Post Assessments of Various Domains

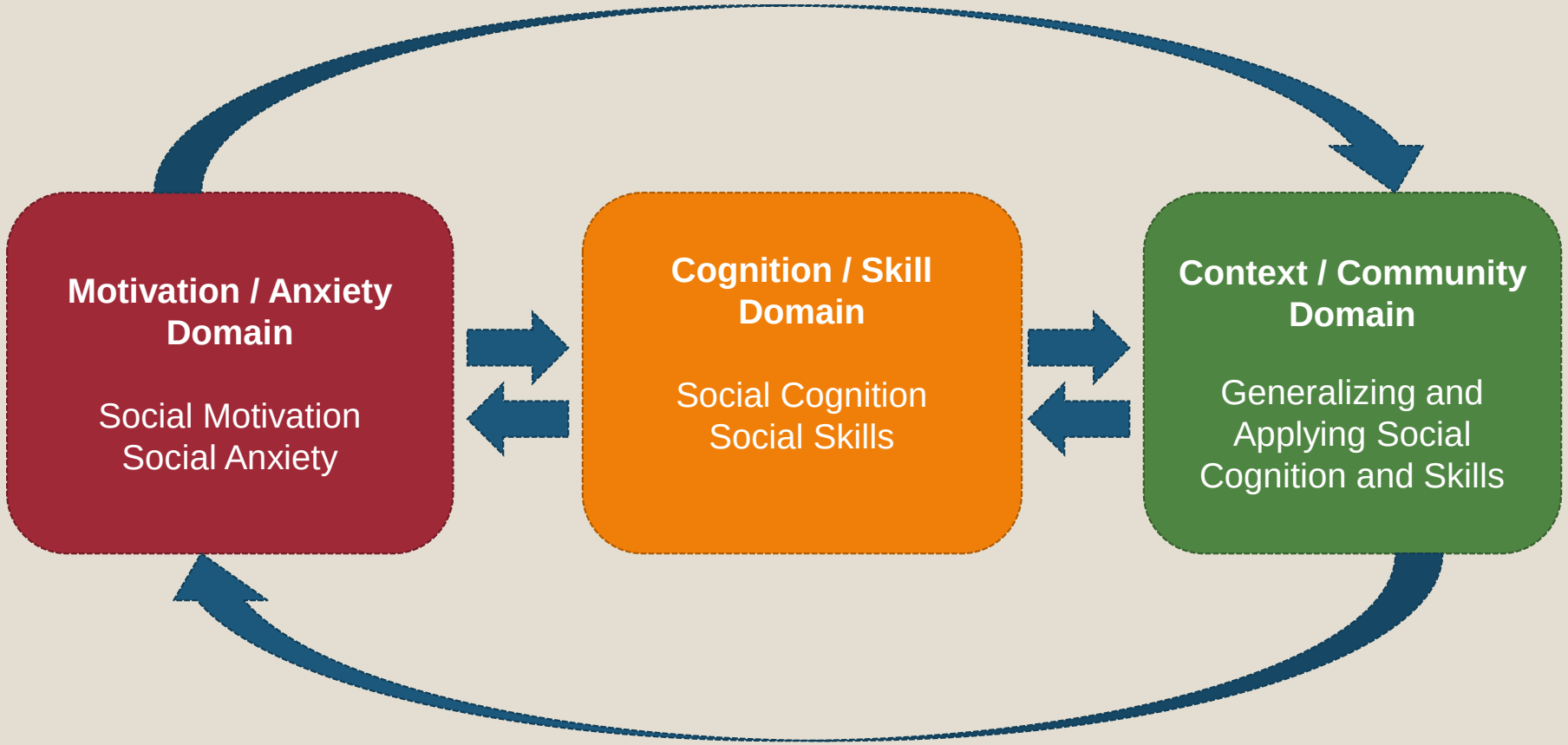
- Overall ASD Symptoms
  - Social Responsiveness Scale, ADOS, SCQ
- Social Motivation
  - Broad Autism Phenotype Questionnaire, MAP-SR
- Social Anxiety
  - Liebowitz Social Anxiety Scale, Schizotypal Personality Questionnaire
- Social Cognition and Attention
  - Penn Social Cognition Battery (ER40, MEDF, ADT), The Hinting Task, Eye Tracking
- Social Skills
  - Contextual Assessment of Social Skills
- Size of Social Network
  - Social Network Index
- Overall Psychological Well Being
  - Scale of Psychological Well-Being

Ashley Pallathra, B.A.

Monica Calkins, Ph.D.

Julia Parish-Morris, Ph.D.

Component 1:
Addressing Social Motivation and Social Anxiety

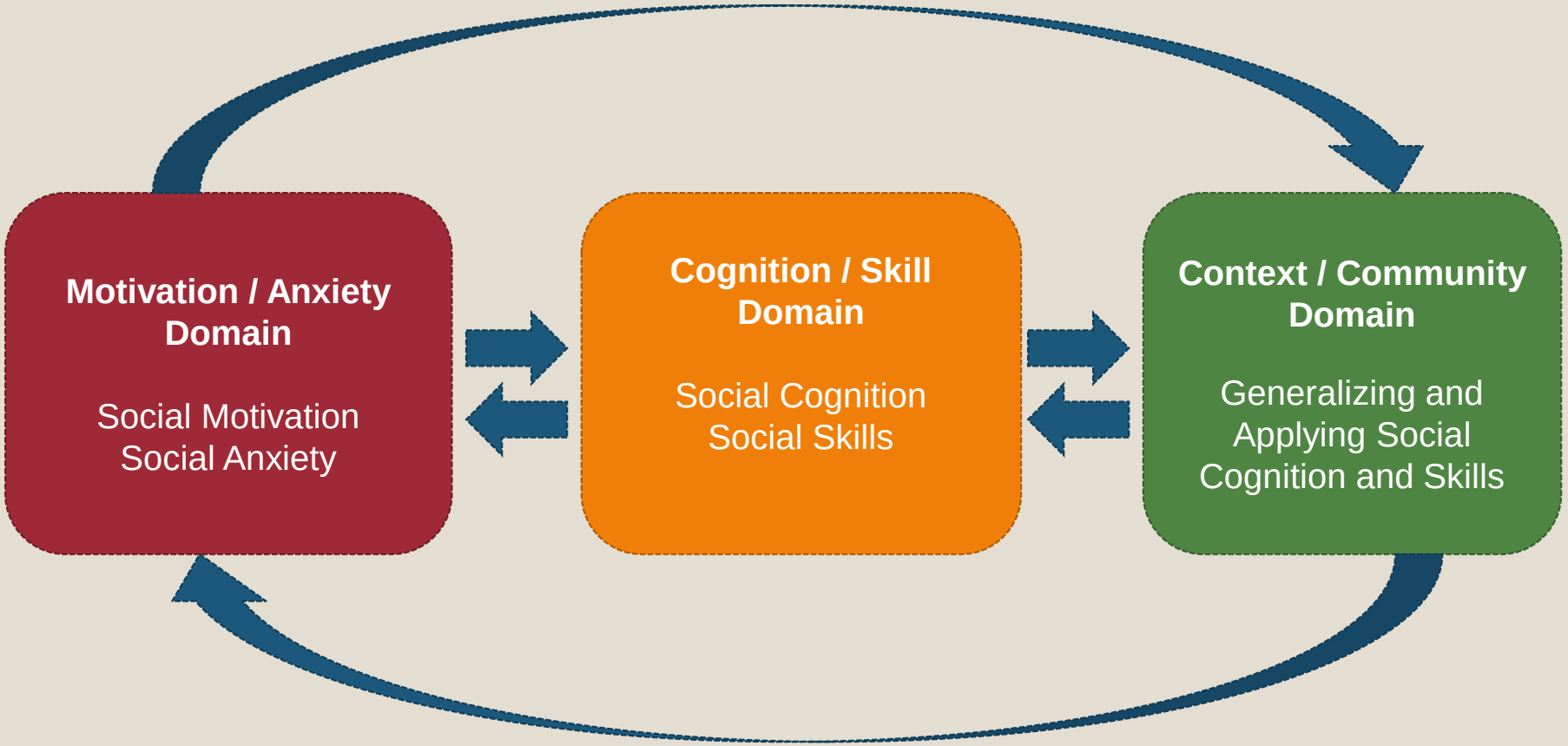


Motivation / Anxiety Domain | Cognition / Skill Domain | Community / Context Domain

Component 1:
Addressing Social Motivation and Social Anxiety

- Once weekly, hour-long individual session for 5 weeks
  - Logistics: Identify and address any logistical / executive functioning hurdles to participating in the program
  - Building motivation: Identify activities that participant finds rewarding, and ways in which improving social functioning can improve his or her ability to engage in those rewarding activities
  - Regulating emotion / social anxiety: Learn and practice mindfulness exercises – reduce social anxiety, manage stress during social interactions (progressive series of exercises from solo to interactive)
  - Cognitive approach to social anxiety: Identify automatic thoughts, feelings, and behaviors that occur during these interactions

Component 2:
Building Social Cognition and Social Skills



Component 2:
Building Social Cognition and Social Skills

- Objectives
  - Didactics: Develop social understanding
    - Where to direct attention
    - How to recognize social and emotional cues
    - Perspective-taking ("Theory of mind")
  - Video modeling of social skills: Develop and practice social skills using video modeling
- Structure
  - Once weekly group sessions for 8 weeks
  - 90 minutes per session
    - 30 minutes of didactic instruction and discussion focused on developing social understanding
    - 60 minutes of video modeling and practice of social skills
  - ~6-8 participants per group

Building Social Skills

- Video Modeling of Social Skills
  - An evidence-based intervention that has proven effective in building social skills in children and adolescents with ASD
  - 40-60 minutes of social skills practice using pre-recorded video models
    - Examples: greeting, maintaining back-and-forth conversation, listening skills
    - Use multiple examples to practice

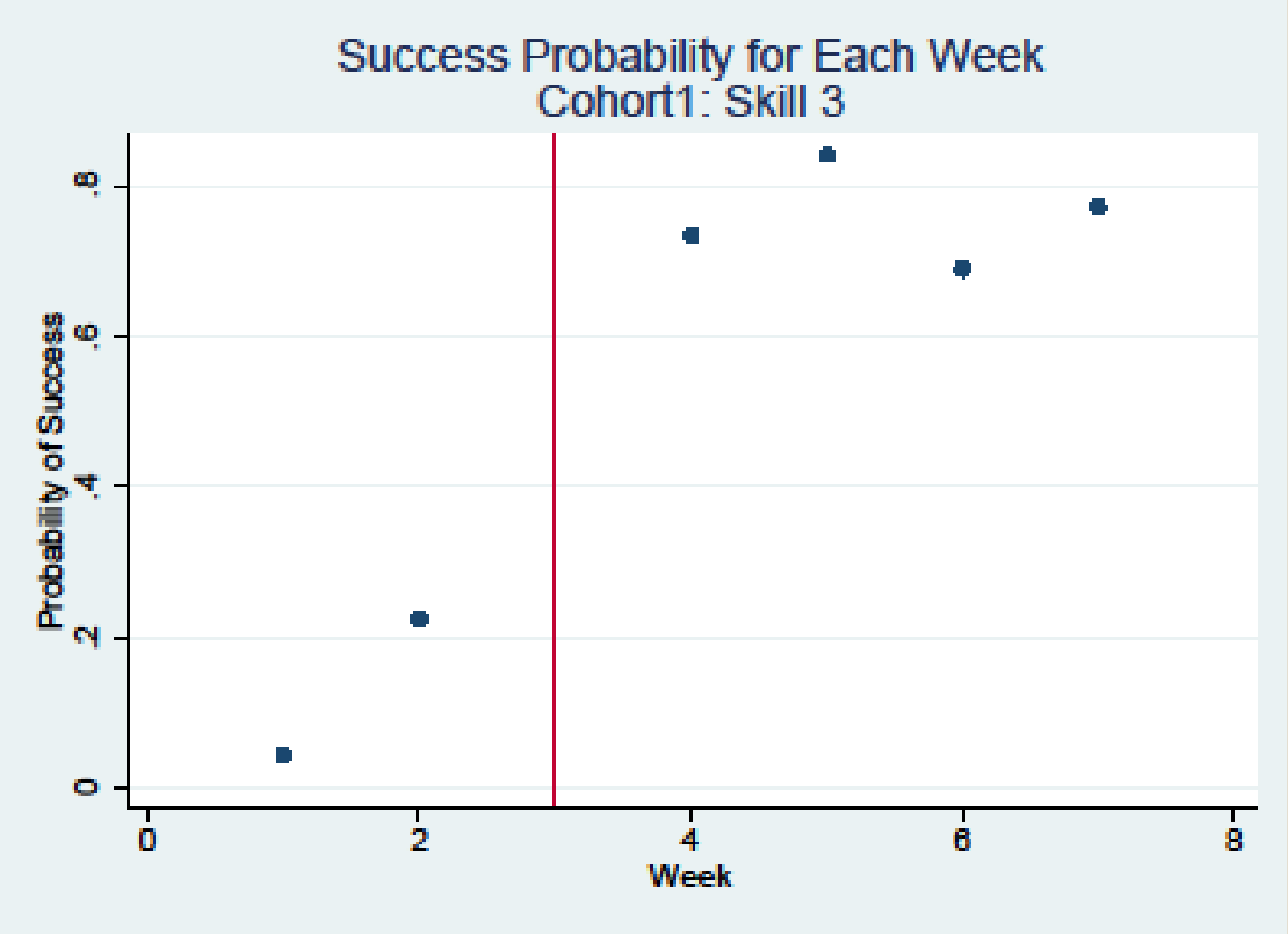
- Collaborators
  - James Connell, PhD. & Jessica Day-Watkins, MSEd, MSEd, BSBA
  - *Drexel University Autism Institute*

Component 2: Social Cognition and Social Skills Group

Ashley Pallathra, B.A.

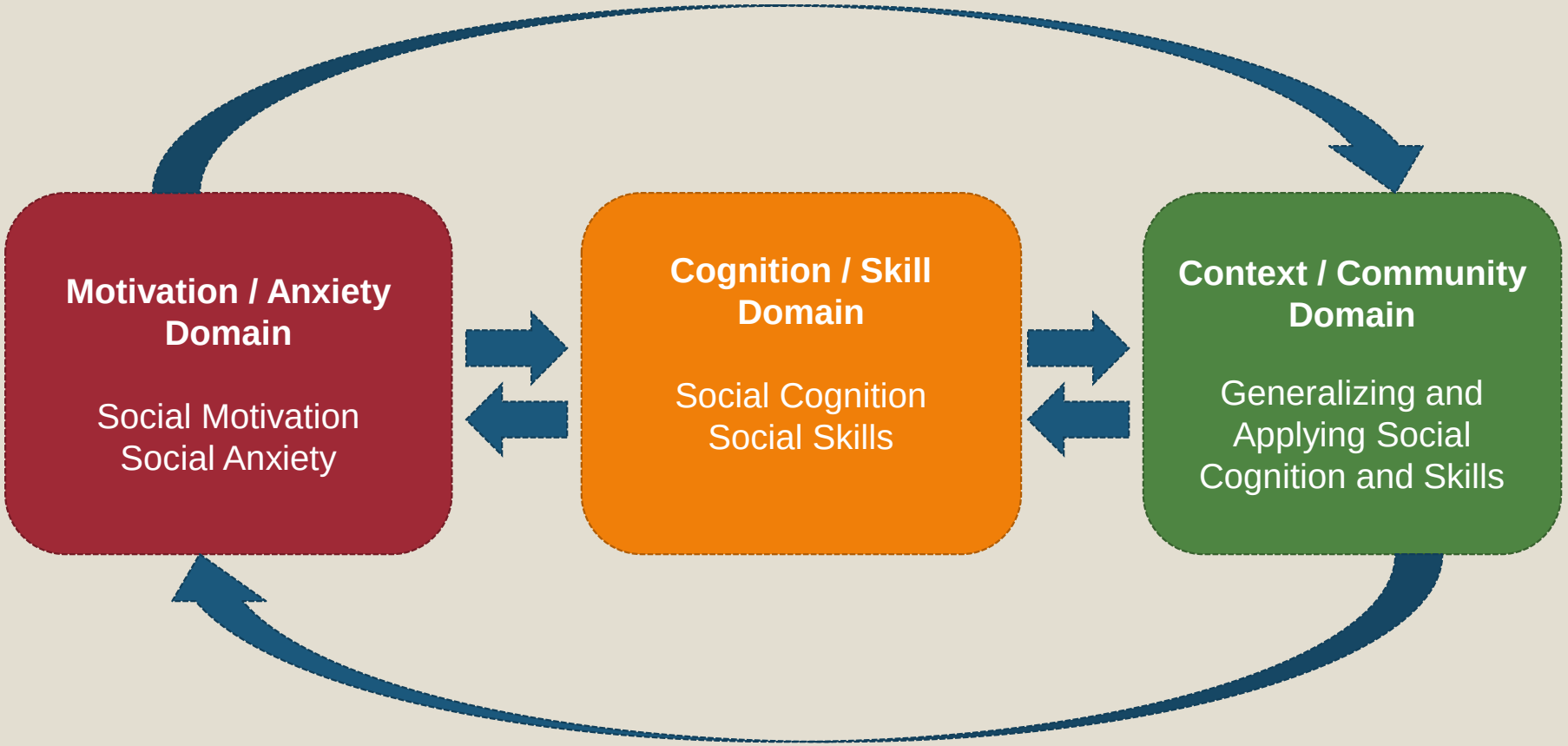
Session	Social Cognition Didactics	Video Modeling of Social Skills
1	Group Introduction to Social Cognition	Baseline Assessment of Social Skills
2	Directed Attention—Distinguishing Social from Nonsocial information	Social Cues Indicating that It Is, or Is Not, a Good Moment to Approach
3	Directed Attention-- Where to Look for Social Information (Facial Expression, Body Language, Direction of Gaze, Tone of Voice)	Social Approach and Greeting
4	Emotion Recognition—Identify Distinguishing Features of Various Emotions	Initiating Conversation
5	Perspective Taking—Catch the Social Cues	Reciprocal Communication: Conversation and Listening Skills, Empathic Responding
6	Emotion Recognition and Perspective Taking	Reciprocal Communication: Conversation and Listening Skills, Empathic Responding
7	Integrating Directed Attention, Emotion Recognition, and Perspective Taking	Reciprocal Communication: Conversation and Listening Skills, Empathic Responding
8	Review, Wrap Up, and Integration of Skills	Putting It All Together: Naturalistic Conversation Practice

Effect of Video Model on Acquisition of Social Approach and Greeting in Cohort 1



Odds ratio 36, $p < 0.05$

Component 3:
Context and Community



Component 3: Generalizing Social Understanding and Social Skills to the Community

- Goals
  - Practice newly acquired social understanding and social skills in a new context -- a “real-world” setting outside of a health care setting
  - Participating on a volunteer work team that is helping others in need

- Structure
  - Site: Ronald McDonald House (3925 Chestnut St., Philadelphia, PA)
  - Work teams consisting of both study participants and typically developing volunteers, including research study personnel
  - 4 sessions; 60-90 minutes per session
  - Assess social understanding and social skill in this setting

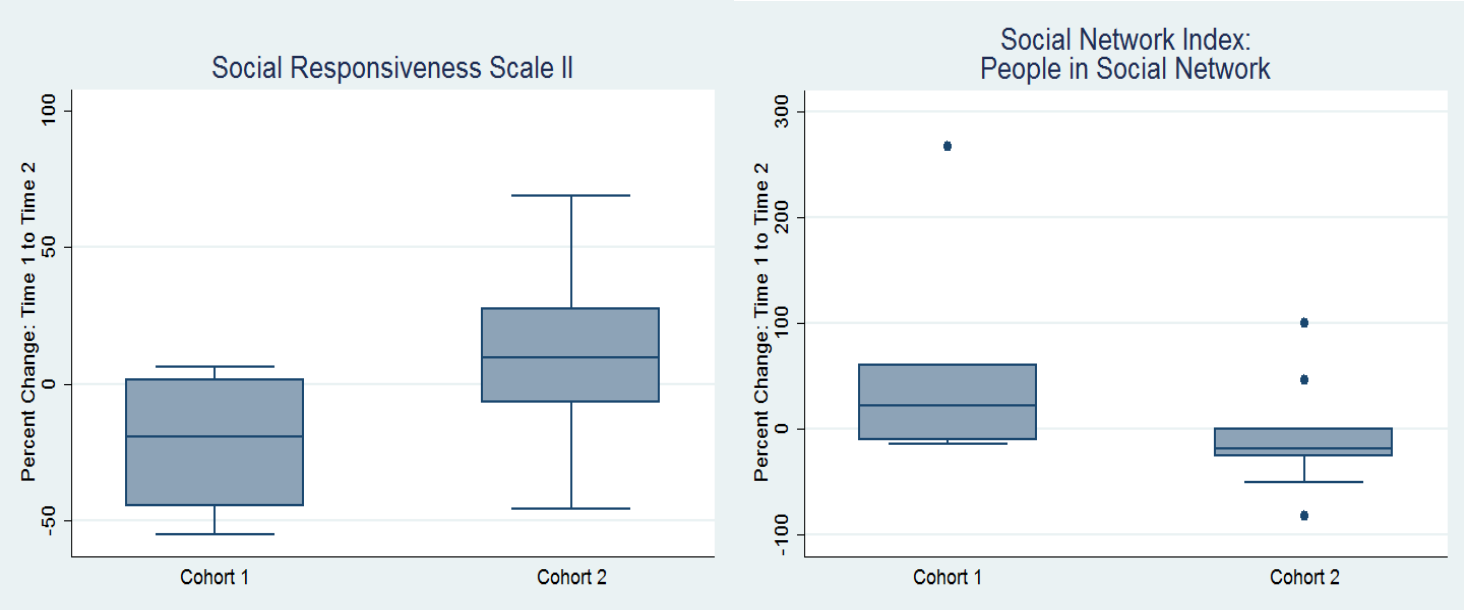
Volunteer Work Team Setting

- Philadelphia Ronald McDonald House (PRMH)
  - 3925 Chestnut St., Philadelphia, PA
  - A philanthropic institution that supports families of seriously ill children
  - Family members stay at the PRMH and have some meals provided to them there
  - Participants are part of a work team that prepares meals for families

Follow Up

- Re-contact participants at 3, 6, and 12 months following the end of the study
  - To determine whether they are still engaged in volunteer work
  - Inquire about employment status
  - Inquire about participation in vocational rehabilitation

Effects of TUNE In on Social Functioning: Preliminary Results



Treatment Wait list Treatment Wait list

Social Responsiveness Scale II (SRS-II)

Social Network Index (SNI)– # of people that participant is in regular contact with

Wilcoxon Rank Sum Test: SRS-II p = 0.03; SNI p = 0.02

Future Directions

- Complete data analysis for Cohorts 1 and 2
- Refine the procedures based on the experience and data from this pilot study
- Larger-scale clinical trials with a larger number of participants to more fully test the treatment
- If effective, dissemination to community mental health providers
- Develop more advanced modules for development of social understanding and social skills
- Develop a program that suitable for intellectually-disabled participants

Our Team

Ted Brodkin, M.D.

Ashley Pallathra, B.A.

Shreya Kangovi, M.D.

Rachel Tomlinson, M.Ed.

Torrey Creed, Ph.D.

Monica Calkins, Ph.D.

Jessica Day-Watkins, MSEd

James Connell, Ph.D.

Femida Handy, Ph.D.

Gabriel Dichter, Ph.D.

Our Team (continued)
Grant and Institutional Acknowledgements

Judith Miller, Ph.D.

Brenna Maddox, Ph.D.

Robert Schultz, Ph.D.

Julia Parish-Morris, Ph.D.

David Mandell, Sc.D.

Connor Kerns, Ph.D.

Grant and Institutional Support

- NIMH grant R34MH104407, “Services to Enhance Social Functioning in Adults with Autism Spectrum Disorder”, Principal Investigator: **Brodkin**

- ITMAT Award in Maturational Human Biology, “Maturational Biology of Social Attention in Autism Spectrum Disorder”, Principal Investigators: **Brodkin and Schultz**

- Department of Psychiatry, Perelman School of Medicine at the University of Pennsylvania
- Center for Autism Research (CAR) at Children’s Hospital of Philadelphia (CHOP)
- A.J. Drexel Autism Institute at Drexel University
- University of North Carolina

Meeting of the IACC

Morning Agenda - continued

11:30 **Committee Business**

Susan Daniels, Ph.D.
Director, OARC, NIMH and Executive Secretary, IACC

Julianna Rava, M.P.H
Science Policy Analyst, OARC, NIMH

12:00 PM **Lunch**

IACC Committee Business

Susan A. Daniels, Ph.D.
Director, Office of Autism Research Coordination
Executive Secretary, IACC
National Institute of Mental Health

IACC Full Committee Meeting
April 26, 2017

IACC
INTERAGENCY AUTISM COORDINATING COMMITTEE

OFFICE OF AUTISM RESEARCH COORDINATION
NATIONAL INSTITUTES OF HEALTH

Susan Daniels, Ph.D., Director

Oni Celestin, Ph.D., Science Policy Analyst

Ben Feldman, M.A., Ph.D., Science Policy Analyst

Rebecca Martin, M.P.H., Public Health Analyst

Angelice Mitrakas, **B.A.**, Management Analyst

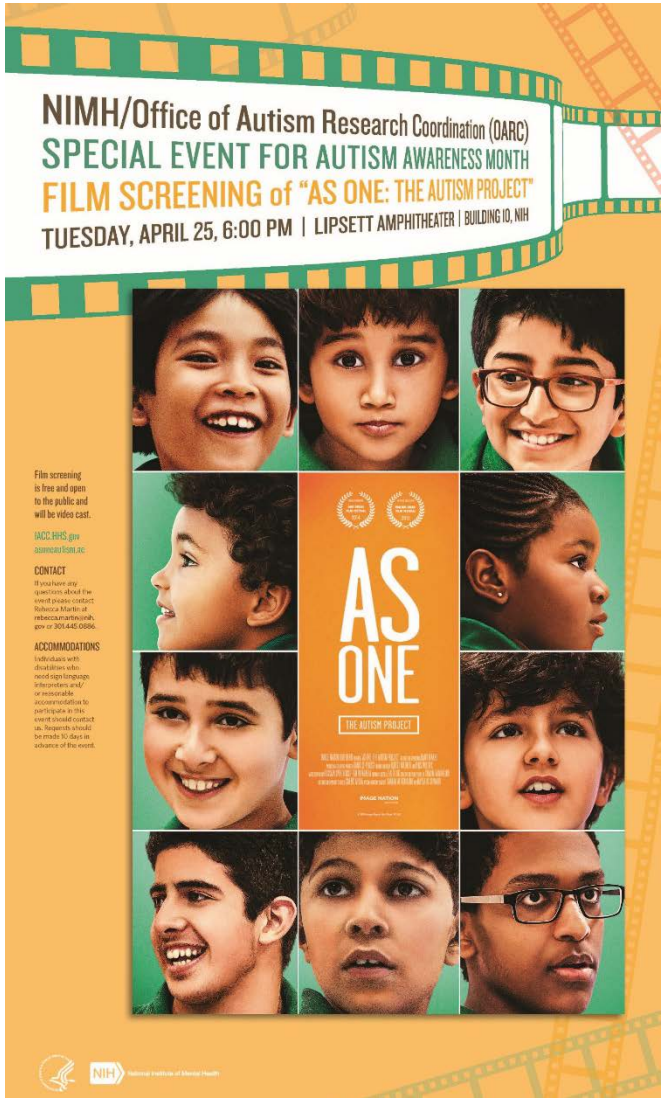
Karen Mowrer, Ph.D., Science Policy Analyst

Julianna Rava, M.P.H., Science Policy Analyst

Jeff Wiegand, **B.S.**, Web Development Manager

April is Autism Awareness Month

NIMH Special Event for Autism Awareness Month



Film Screening of "As One: The Autism Project"

Tuesday, April 25

Image Nation has kindly made free access to the film available through August 22, 2017

https://iacc.hhs.gov/

National Autism Awareness Month Events

Other recent events:

- **March 31, NY - UN World Autism Awareness Day Event: Toward Autonomy and Self-Determination**

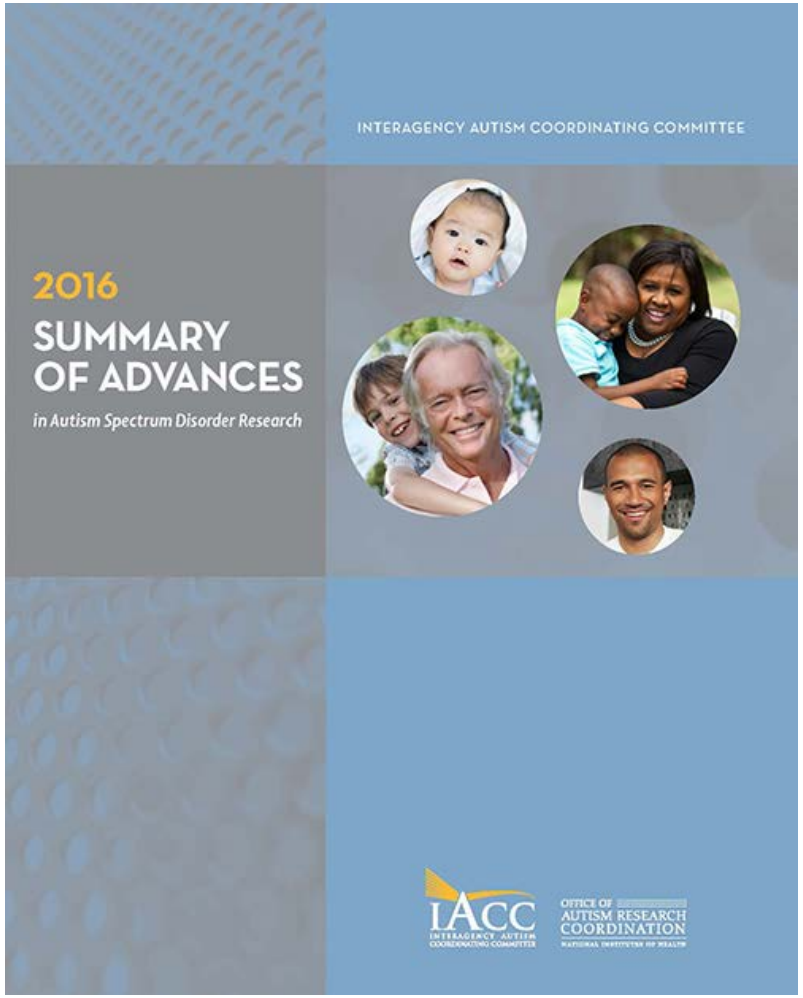
- **April 20, Atlanta - CDC Autism Awareness Month Event that featured a lecture by Daniel Share Strom, A panel on transition to adulthood, and an improvisation performance**

- **As well as events sponsored by other agencies and organizations worldwide.**

National Autism Awareness Month News

- Statement of U.N. Secretary-General for World Autism Awareness Day 2017, **Secretary-General António Guterres**
- Presidential Proclamation: World Autism Awareness Day, 2017, **President Donald J. Trump**
- Autism Awareness Month: Genes and Development in Autism Spectrum Disorder, **Dr. Joshua Gordon, Director, NIMH and Chair, IACC**
- Youth With Autism Spectrum Disorder Transitioning To Adulthood, **Robin Harwood, Health Scientist and Tom Novotny, Deputy Assistant Secretary for Health**

2016 IACC Summary of Advances



- **Annual publication – required by CARES Act**
- **Lay-friendly summaries of the 20 most significant advances in ASD biomedical and services research, as selected by the IACC**
- **Covers articles aligning with all seven Strategic Plan Question areas**

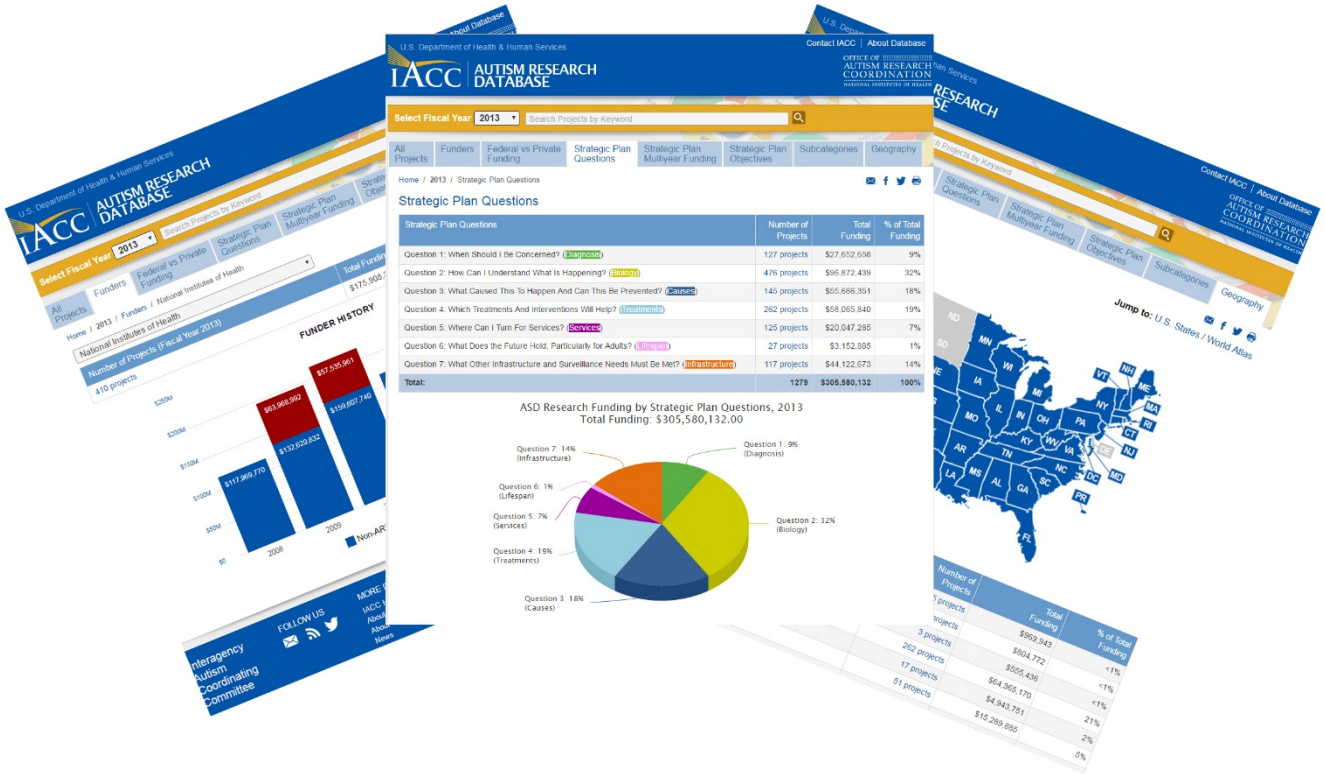
https://iacc.hhs.gov/publications/summary-of-advances/2016/

2013 IACC Portfolio Analysis Report

- **Assists the IACC in fulfilling the CARES Act requirement to monitor Federal activities related to Autism Spectrum Disorder (ASD)**
- **Provides detailed analysis of the ASD research portfolio across both federal agencies and private organizations**
- **Informs the IACC and stakeholders about the funding landscape and current directions in ASD research**
- **Helps the IACC monitor progress in fulfilling the objectives of the IACC Strategic Plan**

https://iacc.hhs.gov/portfolio-analysis/2013/index.shtml

Autism Research Database

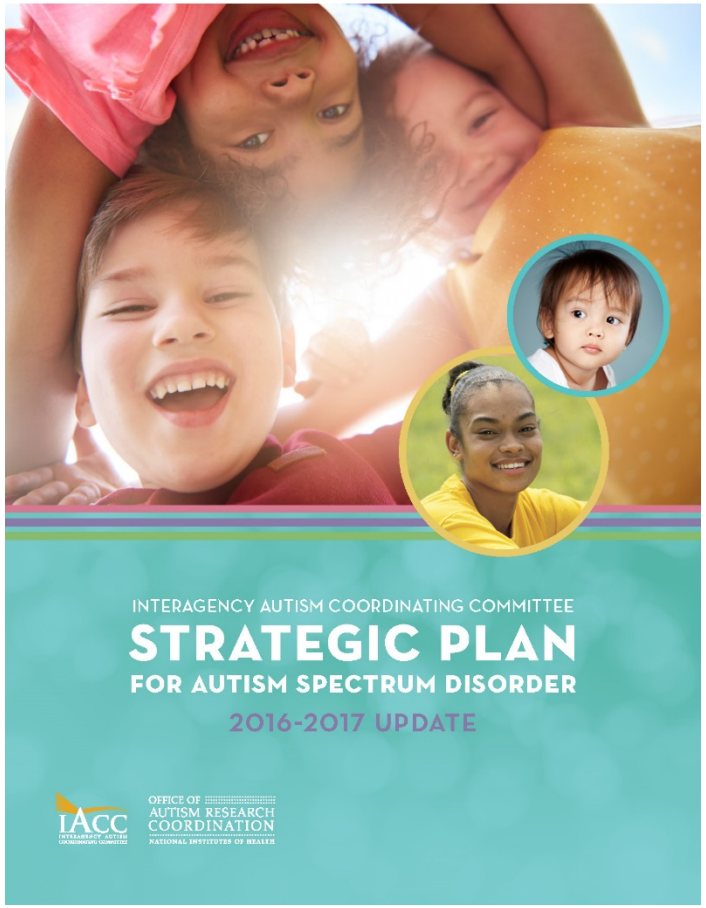


- **A newly designed online database of ASD research**
- **Replaces the *IACC/OARC Autism Spectrum Disorder Research Portfolio Analysis Web Tool***
- **New features: federal vs. private funding; geography**
- **Includes release of the *2013 ASD Research Portfolio Analysis* data**

https://iacc.hhs.gov/funding/data/

IACC Strategic Plan Update

IACC Strategic Plan Update



- **The IACC Strategic Plan (SP) provides a blueprint to guide autism-related efforts across federal agencies and partner private organizations.**
- **The IACC SP is organized around 7 consumer-based questions.**
- **The first IACC SP was developed in 2009 and focused on research efforts.**
- **Under the Autism CARES Act, the new IACC Strategic Plan will address both research and services activities.**

Working Group Activities

- **The IACC formed 7 Working Groups to address the 7 chapters of the Strategic Plan.**
- **Drafts of the 7 chapters have been completed by the Working Groups, including:**
  - **Revised titles and aspirational goals**
  - **Three broad objectives for each Question**
  - **Overview of progress, gaps, opportunities, and needs**
- **Drafts of the 7 chapters have been shared with The Committee for review**

Strategic Plan Issues for Discussion

- Q1:
- Q2: Overlap between Q2 and Q3?
- Q3: Prevention of ASD vs. prevention of disabling aspects of ASD
- Q4:
- Q5: Housing, person centered planning
- Q6:
- Q7:

- Other items?

Q1. When should I be concerned?

nature

Feb 2017

Early brain development in infants at high risk for autism spectrum disorder

Hazlett HC, Gu H, Munsell BC, Kim SH, Styner M, Wolff JJ, Elison JT, Swanson MR, Zhu H, Botteron KN, Collins DL, Constantino JN, Dager SR, Estes AM, Evans AC, Fonov VS, Gerig G, Kostopoulos P, McKinstry RC, Pandey J, Paterson S, Pruett JR, Schultz RT, Shaw DW, Zwaigenbaum L, Piven J; IBIS Network; Clinical Sites; Data Coordinating Center; Image Processing Core; Statistical Analysis.

Molecular Autism

Mar 2017

Neural circuitry at age 6 months associated with later repetitive behavior and sensory responsiveness in autism

Wolff JJ, Swanson MR, Elison JT, Gerig G, Pruett JR Jr, Styner MA, Vachet C, Botteron KN, Dager SR, Estes AM, Hazlett HC, Schultz RT, Shen MD, Zwaigenbaum L, Piven J; IBIS Network.

Q2. How can I understand what is happening?

JAMA Psychiatry
Formerly *Archives of General Psychiatry*

Apr 2017

Association between the probability of autism spectrum disorder and normative sex-related phenotypic diversity in brain structure

Ecker C, Andrews DS, Gudbrandsen CM, Marquand AF, Ginestet CE, Daly EM, Murphy CM, Lai MC, Lombardo MV, Ruigrok AN, Bullmore ET, Suckling J, Williams SC, Baron-Cohen S, Craig MC, Murphy DG; Medical Research Council Autism Imaging Multicentre Study (MRC AIMS) Consortium.

nature COMMUNICATIONS

Feb 2017

Enhanced expression of ADCY1 underlies aberrant neuronal signalling and behaviour in a syndromic autism model

Sethna F, Feng W, Ding Q, Robison AJ, Feng Y, Wang H.

Q3. What caused this to happen and can it be prevented?

Apr 2017

Refining the role of de novo protein-truncating variants in neurodevelopmental disorders by using population reference samples

Kosmicki JA, Samocha KE, Howrigan DP, Sanders SJ, Slowikowski K, Lek M, Karczewski KJ, Cutler DJ, Devlin B, Roeder K, Buxbaum JD, Neale BM, MacArthur DG, Wall DP, Robinson EB, Daly MJ.

Feb 2017

Maternal immunoreactivity to herpes simplex virus 2 and risk of autism spectrum disorder in male offspring

Mahic M, Mjaaland S, Bøvelstad HM, Gunnes N, Susser E, Bresnahan M, Øyen AS, Levin B, Che X, Hirtz D, Reichborn-Kjennerud T, Schjølberg S, Roth C, Magnus P, Stoltenberg C, Surén P, Hornig M, Lipkin WI.

Q3. What caused this to happen and can it be prevented?

Feb 2017

Sex-specific gene-environment interactions underlying ASD-like behaviors

Schaafsma SM, Gagnidze K, Reyes A, Norstedt N, Månsson K, Francis K, Pfaff DW.

Apr 2017

Targeted sequencing identifies 91 neurodevelopmental-disorder risk genes with autism and developmental-disability biases

Stessman HA, Xiong B, Coe BP, Wang T, Hoekzema K, Fenckova M, Kvarnung M, Gerdts J, Trinh S, Cosemans N, Vives L, Lin J, Turner TN, Santen G, Ruivenkamp C, Kriek M, van Haeringen A, Aten E, Friend K, Liebelt J, Barnett C, Haan E, Shaw M, Gecz J, Anderlid BM, Nordgren A, Lindstrand A, Schwartz C, Kooy RF, Vandeweyer G, Helsmoortel C, Romano C, Alberti A, Vinci M, Avola E, Giusto S, Courchesne E, Pramparo T, Pierce K, Nalabolu S, Amaral DG, Scheffer IE, Delatycki MB, Lockhart PJ, Hormozdiari F, Harich B, Castells-Nobau A, Xia K, Peeters H, Nordenskjöld M, Schenck A, Bernier RA, Eichler EE.

Q3. What caused this to happen and can it be prevented?

Molecular Psychiatry

Nov 2016 [Epub ahead of print]

Gestational vitamin D deficiency and autism-related traits: the Generation R Study

Vinkhuyzen AA, Eyles DW, Burne TH, Blanken LM, Kruithof CJ, Verhulst F, Jaddoe VW, Tiemeier H, McGrath JJ.

nature neuroscience

Apr 2017

Whole genome sequencing resource identifies 18 new candidate genes for autism spectrum disorder

Yuen RKC, Merico D, Bookman M, L Howe J, Thiruvahindrapuram B, Patel RV, Whitney J, Deflaux N, Bingham J, Wang Z, Pellecchia G, Buchanan JA, Walker S, Marshall CR, Uddin M, Zarrei M, Deneault E, D'Abate L, Chan AJ, Koyanagi S, Paton T, Pereira SL, Hoang N, Engchuan W, Higginbotham EJ, Ho K, Lamoureux S, Li W, MacDonald JR, Nalpathamkalam T, Sung WW, Tsoi FJ, Wei J, Xu L, Tasse AM, Kirby E, Van Etten W, Twigger S, Roberts W, Drmic I, Jilderda S, Modi BM, Kellam B, Szego M, Cytrynbaum C, Weksberg R, Zwaigenbaum L, Woodbury-Smith M, Brian J, Senman L, Iaboni A, Doyle-Thomas K, Thompson A, Chrysler C, Leef J, Savion-Lemieux T, Smith IM, Liu X, Nicolson R, Seifer V, Fedele A, Cook EH, Dager S, Estes A, Gallagher L, Malow BA, Parr JR, Spence SJ, Vorstman J, Frey BJ, Robinson JT, Strug LJ, Fernandez BA, Elsabbagh M, Carter MT, Hallmayer J, Knoppers BM, Anagnostou E, Szatmari P, Ring RH, Glazer D, Pletcher MT, Scherer SW.

Q4. Which treatments and interventions will help?

Journal of Child and Adolescent Psychopharmacology (JCAP)

Mar 2017 [Epub ahead of print]

Repetitive transcranial magnetic stimulation for the treatment of executive function deficits in autism spectrum disorder: clinical trial approach

Ameis SH, Daskalakis ZJ, Blumberger DM, Desarkar P, Drmic I, Mabbott DJ, Lai MC, Croarkin PE, Szatmari P.

AUTISM RESEARCH

Feb 2017 [Epub ahead of print]

Parent-delivered early intervention in infants at risk for ASD: effects on electrophysiological and habituation measures of social attention

Jones EJ, Dawson G, Kelly J, Estes A, Jane Webb S.

Q4. Which treatments and interventions will help?

Journal of Autism and Developmental Disorders

May 2017

Medical conditions and demographic, service and clinical factors associated with atypical antipsychotic medication use among children with an autism spectrum disorder

Lake JK, Denton D, Lunsky Y, Shui AM, Veenstra-VanderWeele J, Anagnostou E.

PLOS ONE

Feb 2017

Ketogenic diet improves behaviors in a maternal immune activation model of autism spectrum disorder

Ruskin DN, Murphy MI, Slade SL, Masino SA.

Q5. Where can I turn for services?

Apr 2017 [Epub ahead of print]

Brief report: examining the association of autism and adverse childhood experiences in the National Survey of Children's Health: the important role of income and co-occurring mental health conditions

Kerns CM, Newschaffer CJ, Berkowitz S, Lee BK.

Q6. What does the future hold, particularly for adults?

AUTISM RESEARCH

Feb 2017 [Epub ahead of print]

Participation in recreational activities buffers the impact of perceived stress on quality of life in adults with autism spectrum disorder

Bishop-Fitzpatrick L, Smith DaWalt L, Greenberg JS, Mailick MR.

Journal of Autism and Developmental Disorders

Feb 2017

A profile on emergency department utilization in adolescents and young adults with autism spectrum disorders

Liu G, Pearl AM, Kong L, Leslie DL, Murray MJ.

Q6. What does the future hold, particularly for adults?

Psychiatric Services

Mar 2017 [Epub ahead of print]

The transition to the adult health care system among youths with autism spectrum disorder

Nathenson RA, Zablotsky B.

AJPH

May 2017

Injury mortality in individuals with autism

Guan J, Li G.

Q7. What other infrastructure and surveillance needs must be met?

AUTISM RESEARCH

Feb 2017

Prevalence and associated features of autism spectrum disorder in extremely low gestational age newborns at age 10 years

Joseph RM, O'Shea TM, Allred EN, Heeren T, Hirtz D, Paneth N, Leviton A, Kuban KC.

Core Values Statement

Working Group 1 Recommendation:

- Add a value regarding **Equity** in access to screening, diagnosis, and treatment, across race, ethnicity, socioeconomic status, geographic location (rural vs. urban) etc. and that this value affirms a commitment to reduce disparities.

For your reference, the values included in 2011 are:

Sense of Urgency
Excellence
Spirit of Collaboration
Consumer Focus
Partnerships in Action
Accountability

Budget Recommendations

- **Services Budget Recommendations plan**
  - **Developed around 5 areas**
    - **Medicaid**
    - **Tricare**
    - **Private insurance**
    - **Public education**
    - **Vocational rehabilitation**
  - **Timeline developed for inclusion in next SP update**
  - **We will provide updates at future IACC meetings**

Budget Recommendations

- **Research Budget Recommendations plan**
  - **OARC is currently gathering data and performing analyses**
  - **OARC will plan a meeting with the Budget Working Group to discuss**
  - **Narrative with figures will be developed and shared with the IACC before July 2017 meeting**

Strategic Plan: Next Steps

- **Edits and comments from committee due to OARC by May 5**
- **OARC will edit revised drafts and submit to the Full Committee for review; complex edits or concerns may be brought back to WG chairs or IACC chair for resolution**
- **Draft introduction will be revised by OARC and IACC chair to incorporate elements discussed in draft plan and shared**
- **Final document with all sections will be approved at the July IACC meeting.**

Lunch

Meeting of the IACC

Afternoon Agenda

1:00 **Oral Public Comment Session**

1:30 **Summary of Written Public Comments**

1:45 **IACC Committee Member Discussion of Public Comments**

Joshua Gordon, M.D., Ph.D.
Director, NIMH and Chair, IACC

Karen Mowrer. Ph.D.
Science Policy Analyst, NIMH

Meeting of the IACC

Oral Comments Session

I am Alec, Making the impossible, possible.

Hello I am Alec I was born after 10 years of infertility medicine. My brother and I are the 1st IXI babies and I was frozen in a freezer in Brussels Belgium for 1 year and 7 months. You can see the test tube I was made in, my mom helped invent IXI and it used worldwide to make babies.
Until I was 2, we were healthy and happy, then we got poisoned and I stopped talking. That left me with Autism. This is my story….

Some people say I cannot get better, but I do get smarter and healthier every year.
My mom taught me not to give up and to always try new things. I try to do that every day.
Some people ask me who I am and they ask if I am Autistic. I tell them no! I am Alec.

I have Autism but I am a Son, I am a brother, I am a student, I am a scientist
I am an artist, a dancer, I sing before hundreds of people at a time. I help wherever I can.
I won medals and I was the Maryland winner of the PTSA reflections last year.

Some people say I cannot communicate because I am Autistic,
They are wrong, I am Alec, I communicate as a Mascot for my school, a cheerleader and an American by singing the National anthem across the country.
Some people say I do not have feeling and do not understand others feelings because I am Autistic.
No! I am Alec, a boy scout, I take care of people when they get hurt and care for my cats and friends dogs. I am a good friend with a big heart and I have good friends

I want to be part of things and to help and to do things the right way. Sometimes people speak very fast and ask a lot of questions, this can be confusing and I may flap my arms making different sounds. They ask are you Autistic? I say no! I am Alec. I use different ways to say how I feel and I do care for others.
I am nice, I am smart, I am a pool shark
I love to swim and work out at the gym
I enjoy a good book and a museum trip
I enjoy to build and paint and saw, shovel snow and mow the lawn.
No chore is a bore it is one more thing that I can be. I am Alec, that is me.
I learn from the computer and watching others do their jobs and join in too
I ride, my horse, and shoe and groom
Calming him as I sing him a song
I am brave and courageous and perform on stage,
In high school I was the crowd favorite as MR AHS, dancing and singing it was the best.
Biking in the woods and to parks, swinging so high in day and in dark
Roller-skating, golf, tennis and racquetball are some things I do.
Basketball, football, soccer, trampoline and skiing too, bowling is the sport that I do best, I have my own ball and I am set.
I draw and I paint what I see, I have won many shows now that is so neat.
I love to relax in the hot tub and swim and with friends, riding the water slide again and again
When I work at the nursery and a restaurant too, I never stop helping and want to please and do
I teach a dance class and get so much joy, as you can see I do not just have Autism, I am way more!
As the photographer of the yearbook, each photo was perfectly shot and placed thorough out the book there were a lot.
I feed the homeless and dress them too; my mom and I love to help them get out of the blues.

So next time you ask someone who they are, make sure you do not judge by a mar or a scar, not a trait that may look different nor something they can not prevent, look to see the wonderful talents, which are heavens sent.
Look to see talents and to be a friend, forget their challenges and differences again and again.
Celebrate accomplishments and every day feats, you will find more friends and that will be neat.
So before you ask if I am Autistic and look what I cannot do, remember it is the strengths you need to allow to shine through.

Who am I? I am Alec a person who never gives up, a person of strength, feelings, kindness and courage and a person who makes things that appear impossible a reality.
Am I Autistic? No I have Autism, but I am Alec!

Meeting of the IACC

Oral Comments Session

The List of Autism Research in PubMed Google Scholar

- In space of 7 years this agency has spent more than 1.7 billion dollars they did not help our children not even one bit.
- Genetics: 6174 (PubMed), 176,000 (Google Scholar) Articles
- **Somatic mutations reveal a neuron's history, DNA diversity in the brain. We need to support the Brain Bank, MIND Institute and Christopher Walsh, MD, PhD, of Harvard Medical School.**
- Neuroimaging: 2718 (PubMed), 49,200 (Google Scholar) Articles

  Bhil Ali 14196(PbMd) 674000 (Gl

It is Time to Dedicate Resources to a More Fruitful Path; Environmental Causation of Autism

- Among parents by the Simons Foundation found that 42% of parents felt vaccines contributed to their child's autism.
- In 2009 the National Vaccine Advisory Committee (NVAC) recommended to this committee a number of feasible research proposals on vaccines and autism. Not a single one has been implemented. Need of funding is the role of vaccines in autism etiology.
- Vaccinated Vs Unvaccinated Children: Zero Published Articles

Federal Register / Vol. 49, No. 107 / Friday, June 1, 1984 .Final Rules and Regulations

"Any possible doubts, whether or not well founded, about the safety of the vaccine cannot be allowed to exist in view of the need to assure that the vaccine will continue to be used to the maximum extent consistent with the nation's public health objectives".

Vaccine Adverse Events Reporting System (VAERS) and Vaccine Safety Datalink

According to CDC It is estimated that only 1–10% of all physicians report a severe health problem which occurs after a drug or vaccine is given to a patient.

Vaccine Safety Datalink, a collaborative project between CDC and nine integrated health care organizations which links vaccination data to health outcomes and initiates vaccine safety.

Adverse Reaction to Childhood Vaccination

- Death, Brain swelling, Shock, Anaphylaxis, Cardiac arrest, Ataxia, Sudden Infant Death Syndrome, Seizures, Autism, Fever, Insomnia, Narcolepsy, Myalgia, Arthralgia, Urticarial, Edema, Upper respiratory tract infection, Diarrhea, Paralysis, Infertility, Swelling at injection site, Rash, Fatigue, Headache, Nausea, Chills, Guillaine-Barre Syndrome, Drowsiness.
- Over $3.6 billion in federal compensation has already been paid out in awards to vaccine injured victims.

IACC Need to be Recognize its Failure and Restructure

- There is no one to represent severely effected children like my son.
- Reach out to other Autism Organizations.
- Limiting Parents and Autism Organizations in Public Speaking at IACC is wrong and illegal.
- Autism Science Foundation has three representatives. Vaccine Gate Keepers.
- Autism Speaks.

Meeting of the IACC

Oral Comments Session

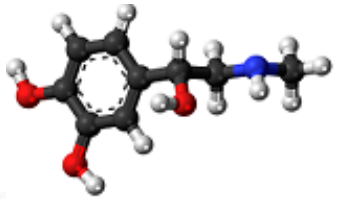
Where is Autism Research leading us?

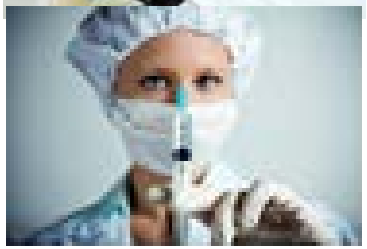
NIH/NIMH/IAAC Full Committee Meeting, April 26, 2016

By Dr. Linda VARSOU-PAPADIMITRIOU

Associate Professor, PhD, MPH, DABCC

Mother and legal guardian of a 31-year-old son with autism





Presentation topics

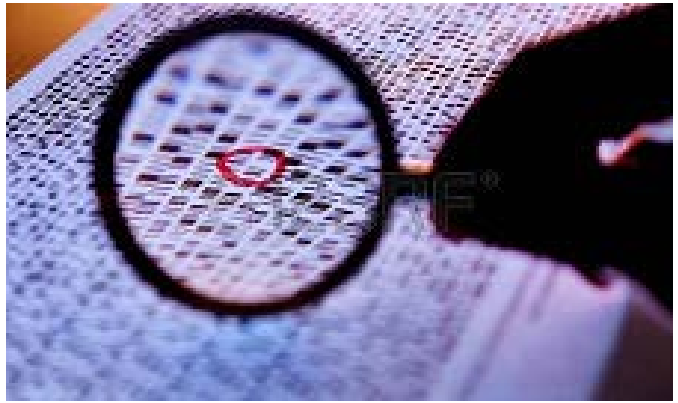
- Genetic studies
- Epigenetics
- Animal studies
- Brain studies
- Immunizations
- Publications

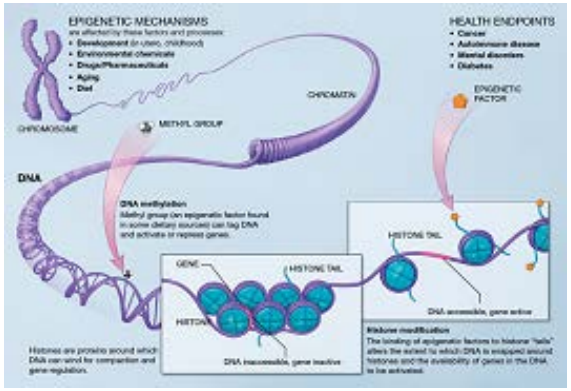
Genetic studies

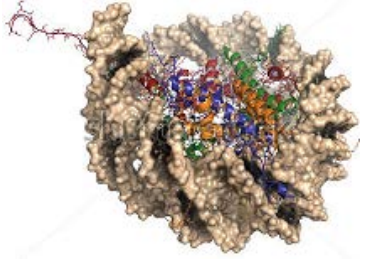
Despite the inherited autistic "traits", genes alone cannot explain the autism epidemic within one generation (25 years).

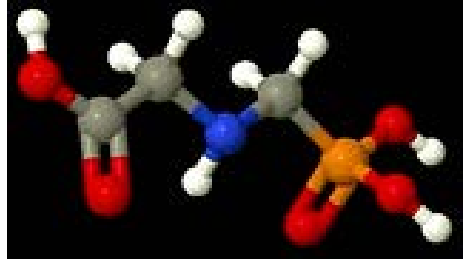
A genetic study needs the "*trio*" (child, mother and father), but the Chronic Parental Denial of child's autism in 50% of families limits the "*trio*" participation in the study, usually of the father.

Therefore, we must look at Epigenetic factors, identify them and try to control and/or to eliminate the dangerous ones







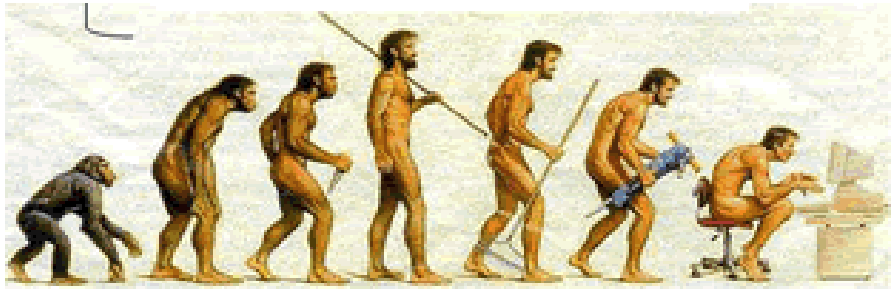


Epigenetics

- **Prenatal factors in the womb**
- **Environmental pollution, chemicals, insecticides**
- **Herbicides, pesticides, drugs, pharmaceuticals**
- **Unhealthy diet, GMOs, unhealthy microbiome**

=

Histones modification & altered gene expression



Animal Studies

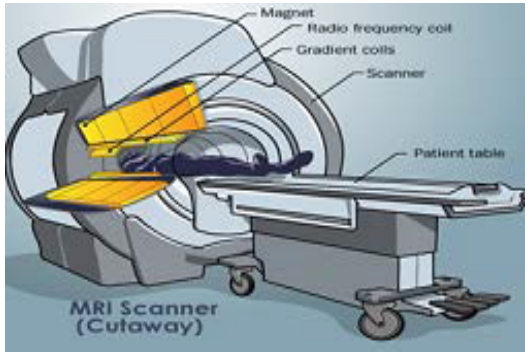
Research on animals can give misleading results.

The immune system of mice significantly differs from humans.

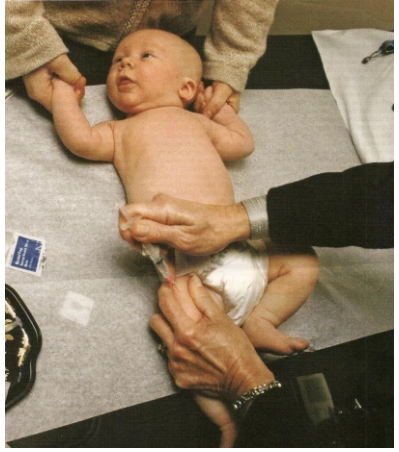
Animal genome is adapted to different environments & needs.

Brain Studies

The Neuroimaging is an extremely invasive technique especially for young brains neurologically compromised. MRI (interventional, real time or functional) produces a huge magnetic field and electromagnetic radiation. It changes Hydrogen electrons' spin and orientation but not all electrons return again to their initial spin. Add on side effects from contrast materials and drugs.



Immunizations (Vaccines)



www.vaxxedthemovie.com

www.vaccinesrevealed.com

www.thetruthaboutvaccines.com

The immune and nervous systems of babies are immature.
At early age, even "safe vaccines" can cause adverse reactions
(like autism, ADHD, lifelong chronic autoimmune diseases, etc.)
due to "immune-deviation" mechanisms in an immature organism.

Publications

The exponential increase of autism publications shows not much positive impact on the lives of people with autism.

Dr. John Ioannidis, M.D., mathematician and epidemiologist, Professor at Stanford University, studying publications says:

“The majority of them fail to provide true findings and solid proof due to many reasons like conflicting or non-reproducible results”

*“**P**” = **p**ressure for **p**apers, In academia:**"publish or perish"***

Different ways of evaluating “ *p* – value “

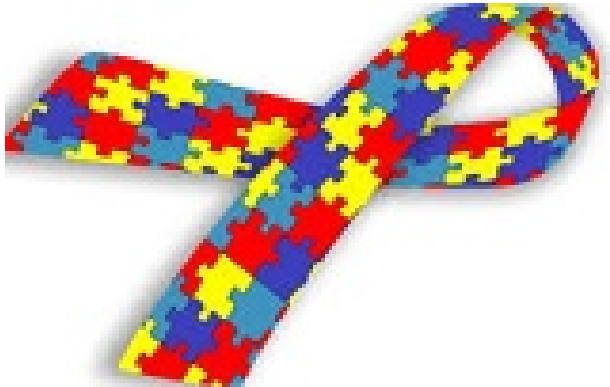
p < 0.00....	**people**
papers	**p**atients
publications	**p**arents
promotion	**p**ain
prestige	**p**ressure
positions	**p**rice
professors	**p**overty
professionals	**p**revalence
praise	**p**revention
power	**p**opulation

Conclusion:
Think about that

Research with positive impact on people with autism and "*An Autism Friendly Society*" will benefit us all.

It is worthy to try and achieve it.

Thank you for your attention



Meeting of the IACC

Oral Comments Session

Meeting of the IACC

Summary of Written Public Comments

These slides do not reflect decisions of the IACC and are for discussion purposes only.

Meeting of the IACC

IACC Committee Member Discussion of Public Comments

These slides do not reflect decisions of the IACC and are for discussion purposes only.

Meeting of the IACC

Afternoon Agenda - continued

2:00 Panel on Advances in Autism Biomarkers Research

2:00 Practical and Scientific Challenges in Biomarker Development for ASD

James McPartland, Ph.D.
Associate Professor of Child Psychiatry and Psychology Director, Yale Development Disabilities Clinic Principal Investigator, Autism Biomarkers Consortium for Clinical Trials, Yale Child Study Center

Practical and scientific challenges in biomarker development for ASD

James C. McPartland, Ph.D.

Associate Professor of Child Psychiatry and Psychology

McPartland Lab (www.mcp-lab.org)

Yale Developmental Disabilities Clinic (www.autism.fm)

Autism Biomarkers Consortium for Clinical Trials (www.asdbiomarkers.org)

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Overview

- Biomarkers
  - Definition
  - Objectives
- Challenges in ASD
- Progress and shortcomings
- Needs for future research
  - More rigorous studies
  - More sensitive biomarkers
  - Practical biomarkers

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Biomarker definition

Any characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention

No clinically practicable biomarkers in ASD

Biomarkers Definition Working Group, 2001

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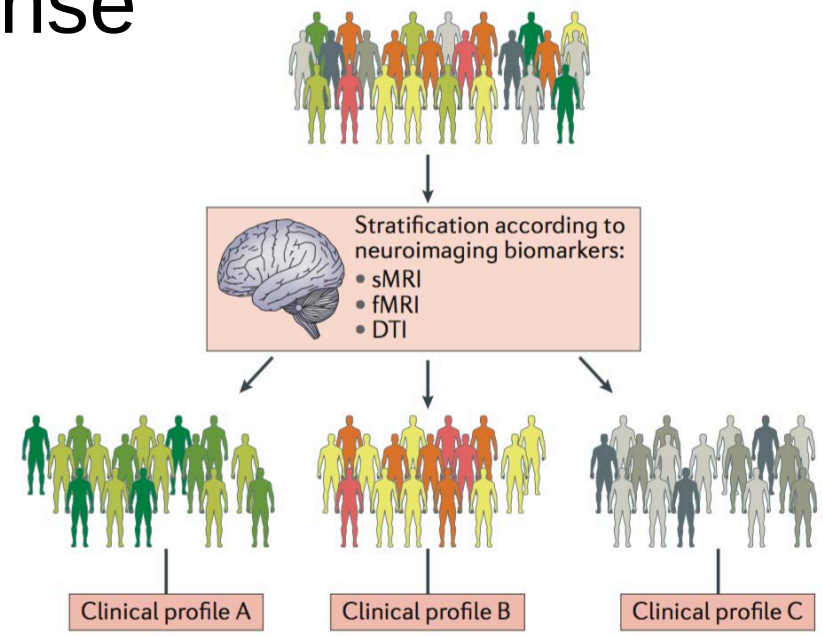
Biomarker objectives

- Diagnosis/screening
- Stratification
  - Treatment selection
  - Prognosis
- Treatment response



Walsh, Elsabbagh, Bolton, Singh, 2011; Loth et al., 2015; McPartland, 2016

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Challenges in ASD

- Behavioral diagnosis
  - Social-communicative impairment
  - Rigid, repetitive behaviors and atypical sensory responses

Developmental change

Multiple etiologies

Heterogeneity

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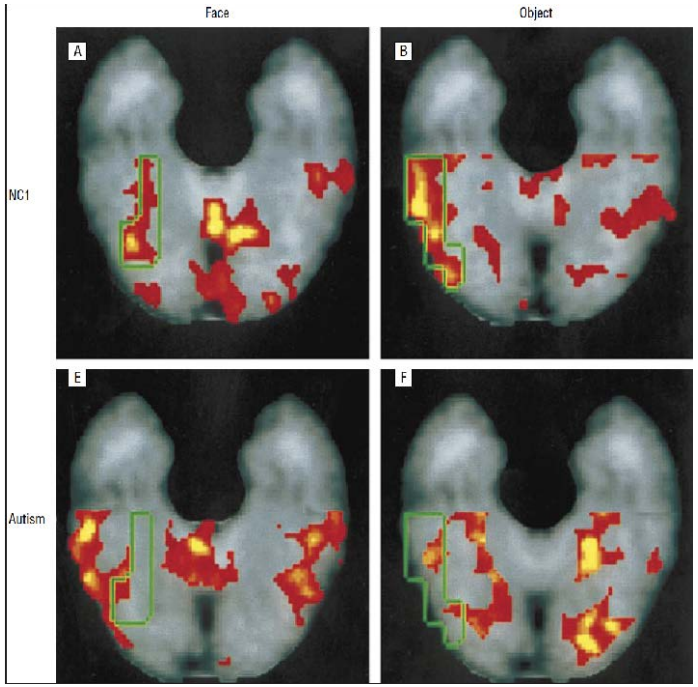
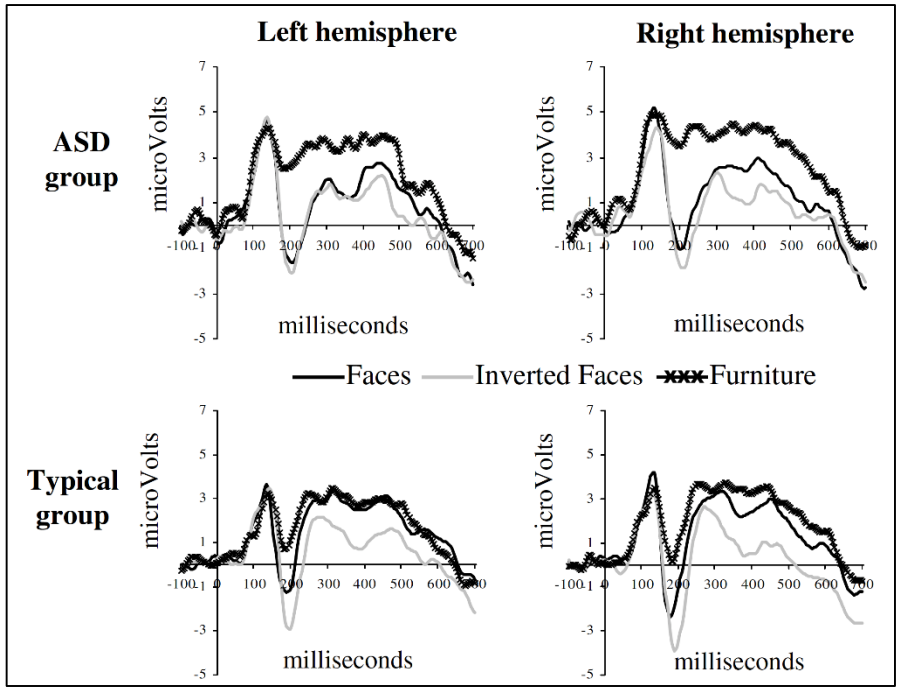
ASD biomarkers: Progress

- Numerous promising biomarkers
  - Neural response to faces
    - fMRI: Fusiform gyrus activation
    - Event-related potential: N170





Schultz et al., 2000 *McPartland et al., 2004*

McPartland et al., 2004; O'Connor et al., 2005, 2007 McPartland et al., 2011; Dawson et al., 2012

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ASD biomarkers: Shortcomings

- Inconsistent reproducibility
  - True heterogeneity in ASD
  - Underpowered studies
  - Methodological variability
  - No frame of reference in typical development

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McPartland et al., 2004, 2011; Grice et al., 2005; O'Connor et al., 2005, 2007; Dawson et al., 2005; Senju et al., 2005; Valdizan, 2005; Kemner et al., 2006; Webb et al., 2006, 2009, 2012; Boeschoten et al., 2007; Gunji et al. , 2009; Magnee et al., 2008; Wong et al., 2008; McCleery et al., 2009; Akechi et al., 2010; Churches et al., 2010, 2012; Hileman et al., 2011; Batty et al., 2011; Apicella et al., 2013; Khorammi et al., 2013; Wagner et al., 2013; Tye et al., 2013, 2014; Cygan et al., 2014; Key et al., 2014

Needs: More rigorous studies

- Larger samples to understand variability
- Tightly controlled methods
- Longitudinal design
- Development of normative “atlas”

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NATIONAL INSTITUTES OF HEALTH

SFARI
SIMONS FOUNDATION AUTISM RESEARCH INITIATIVE

THE biomarkers CONSORTIUM

FNIH
Foundation for the National Institutes of Health

Needs: More sensitive biomarkers

- Questionable ecological validity of social neuroscience methods
- Interactive social neuroscience

Schilbach et al., 2013; Rolison et al., 2015; Naples et al., in press; Hirsch et al., under review

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Needs: Practical biomarkers

- Practicality limits ultimate utility
  - Cost
  - Accessibility

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Acknowledgements

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- ✶Michael Plöchl

Seaver Center
- ✶Alex Kolevzon
- ✶Jen Foss-Feig

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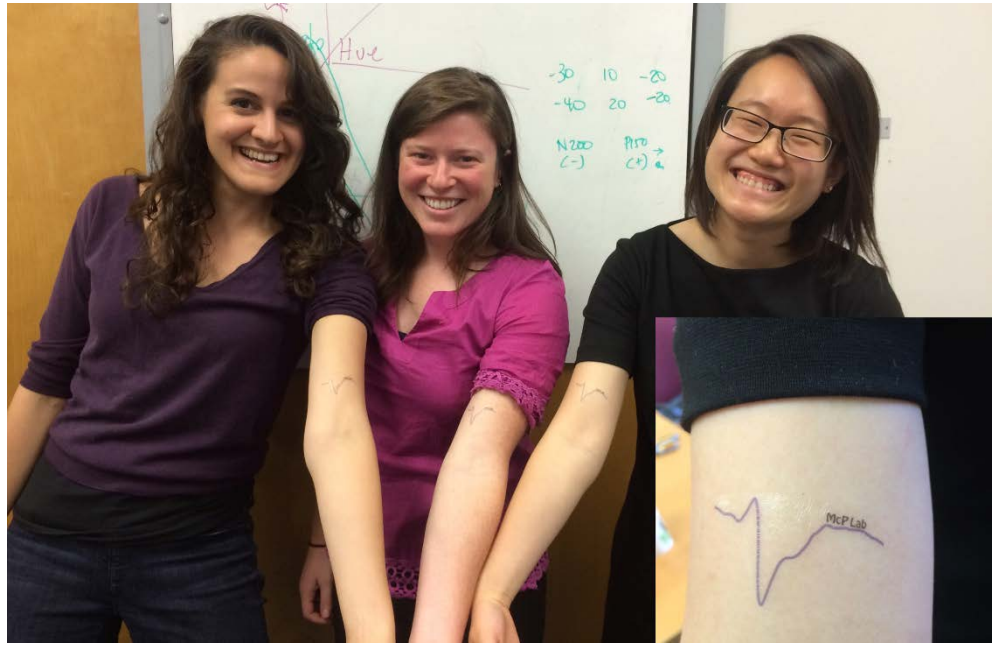

- Adam Naples
- Max Rolison
- Tatiana Winkelman
- Ela Jarzabek
- Takumi McAllister
- Kathryn McNaughton
- Simone Hasselmo
- Taylor Halligan
- Julie Trapani
- Bela Ponjevic
- Erin MacDonnell
- Sabrina Malak
- Talena Day
- Kim Ellison
- Adham Atyabi

- Kayla Stinson
- Brianna Lewis
- Zack Williams
- Alex Sun
- Laura Morett
- Hannah Reed
- Brookie Hewes
- Hannah Tyson
- Julie Wolf
- Monique Staggers
- Nicole Wright
- Scott Jackson
- Ariel Chang
- Celeste Cheung
- Emily Levy
- Hannah Reuman
- Marika Coffman
- Cora Mukerji

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Meeting of the IACC

Afternoon Agenda - continued

2:15 Differences in early brain development predict ASD outcomes in high risk infants

Heather Hazlett, Ph.D.
Assistant Professor of Psychiatry
Carolina Institute for Developmental Disabilities
University of North Carolina School of Medicine

Differences in early brain development predict ASD outcome in high risk infants

Heather Cody Hazlett, PhD

Department of Psychiatry &
Carolina Institute for Developmental Disabilities
University of North Carolina

Meeting of the Interagency Autism Coordinating Committee
Bethesda, MD April 2017

Conflicts of Interest

No conflicts of interest

Research funding support:

Why study early brain development in autism?

Early brain overgrowth

‘infantile autism’
Leo Kanner (1943)

He reported that 5 of the original 11 cases had ‘relatively large heads’

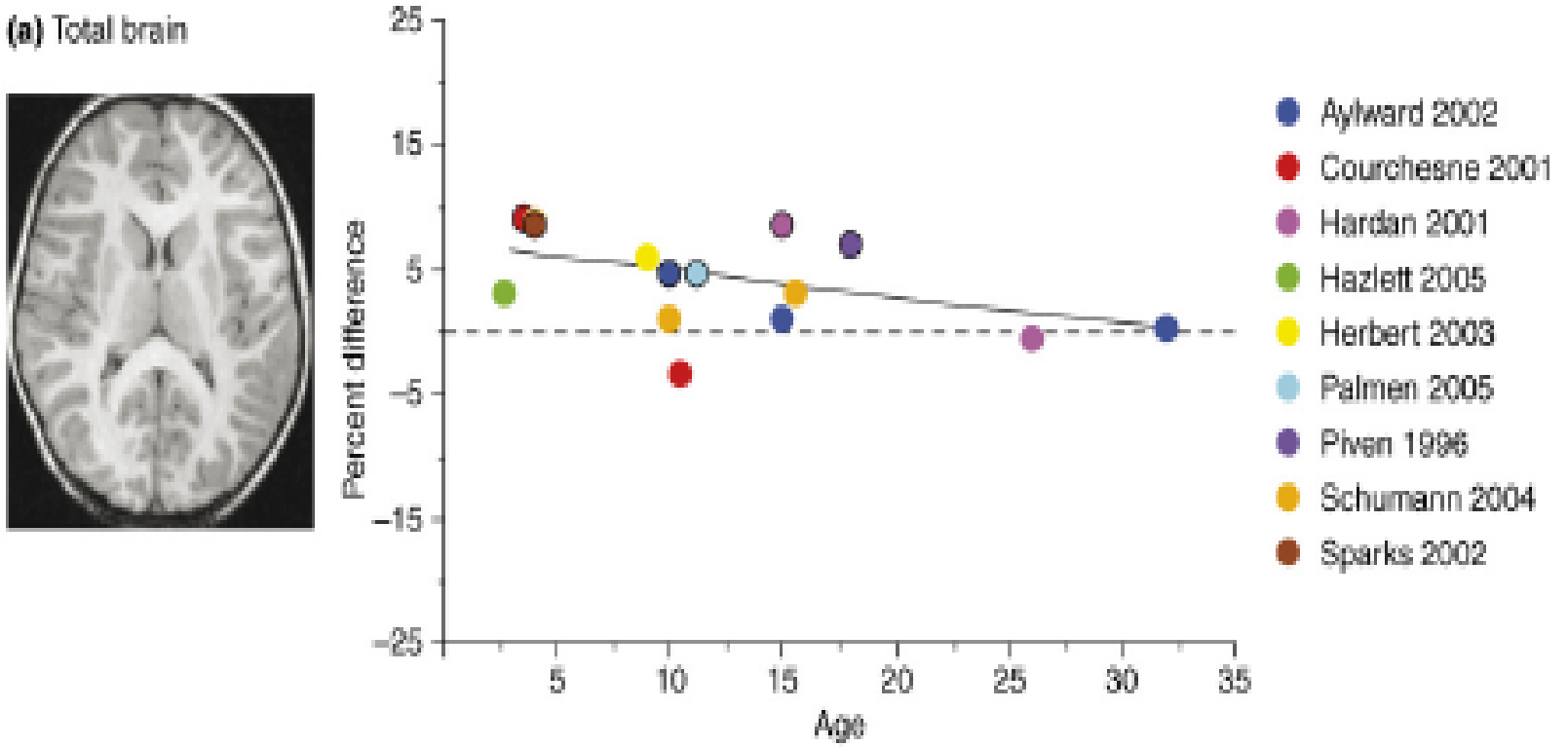
Kanner

Head Circumference

- Indirect measure of brain
- Increased head circumference in ASD, present during the first 3 years
- Methodological differences in studies

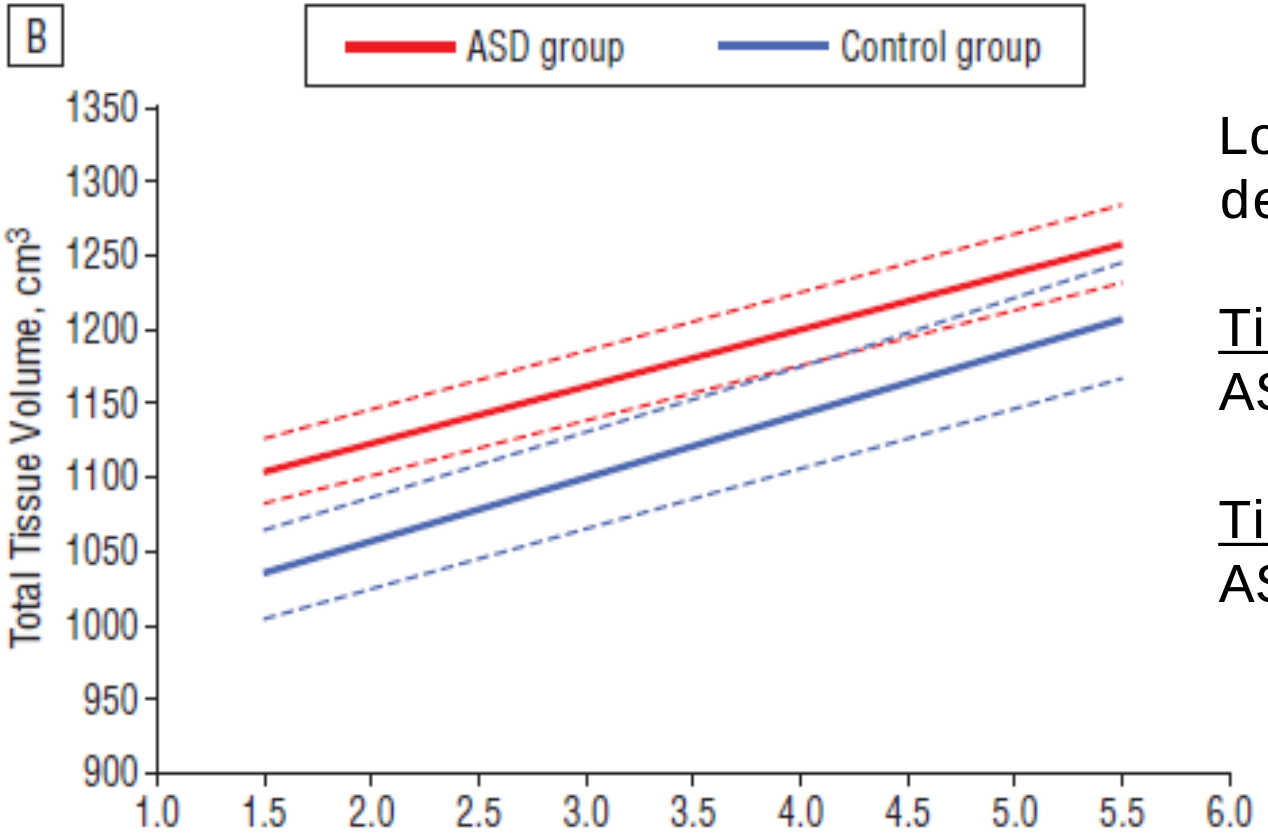
  Prospective/retrospective
  Samples included/diagnostic criteria
  Accuracy of measures/QC
  Normative data

Brain volume increased early in autism



Amaral, Schumann, & Nordahl, 2008

Brain development present in toddlers with ASD



Longitudinal design:

Time1(~ 2 yrs)
ASD=59,TD=38

Time (~ 4-5 yrs)
ASD=36,TD=21

Hazlett et al., Am J Psych, 2011

Increased surface area, but not cortical thickness, in a subset of young boys with autism spectrum disorder.

Ohta, Nordahl, Iosif, Lee, Rogers, & Amaral. Autism Res, 2015.

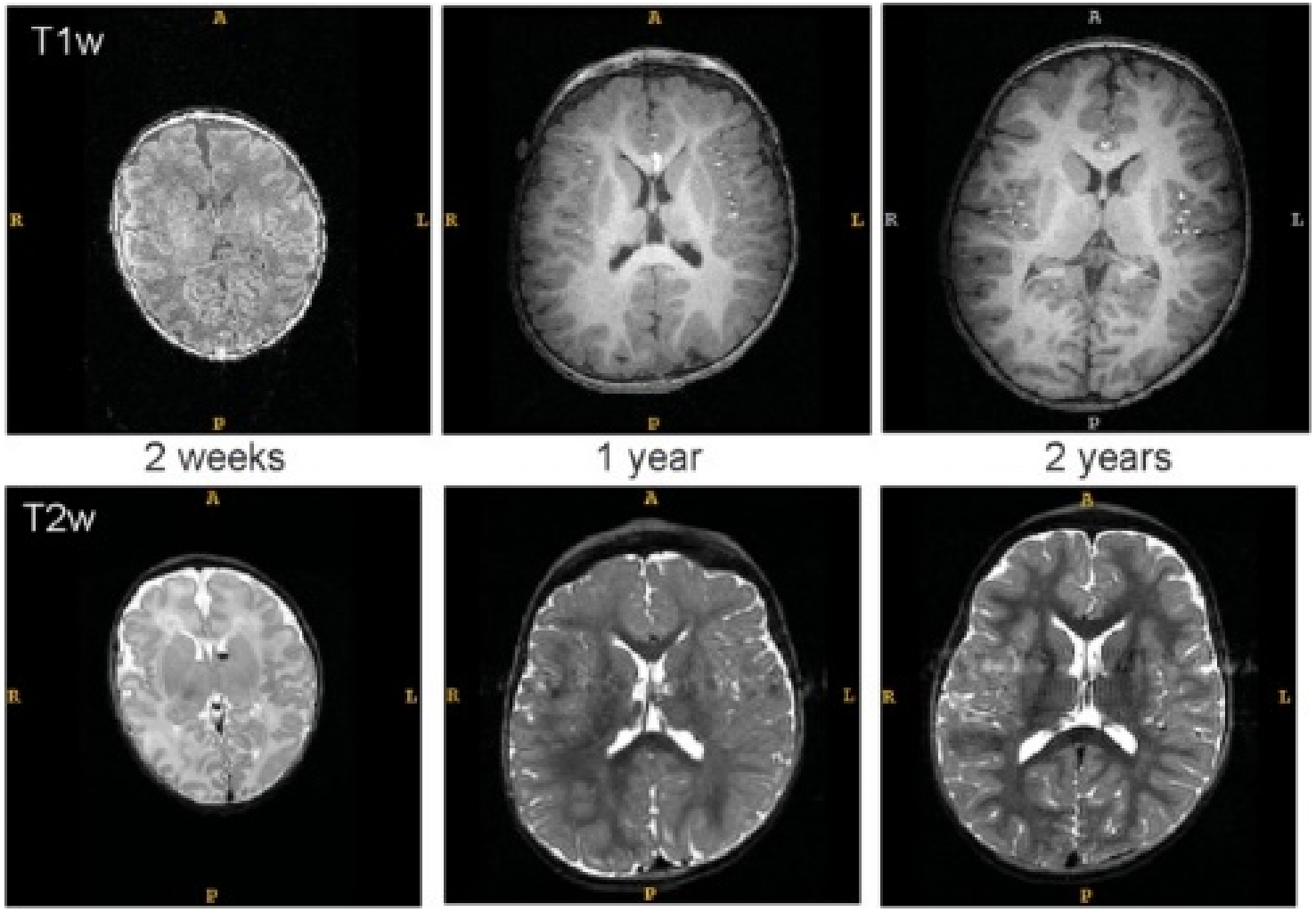
- Autism Phenome Project
- 115 ASD boys (15% DM), 50 TD boys
- Scanned at age 3

- Found ASD group had greater surface area than TD but not in cortical thickness

Birth to Three

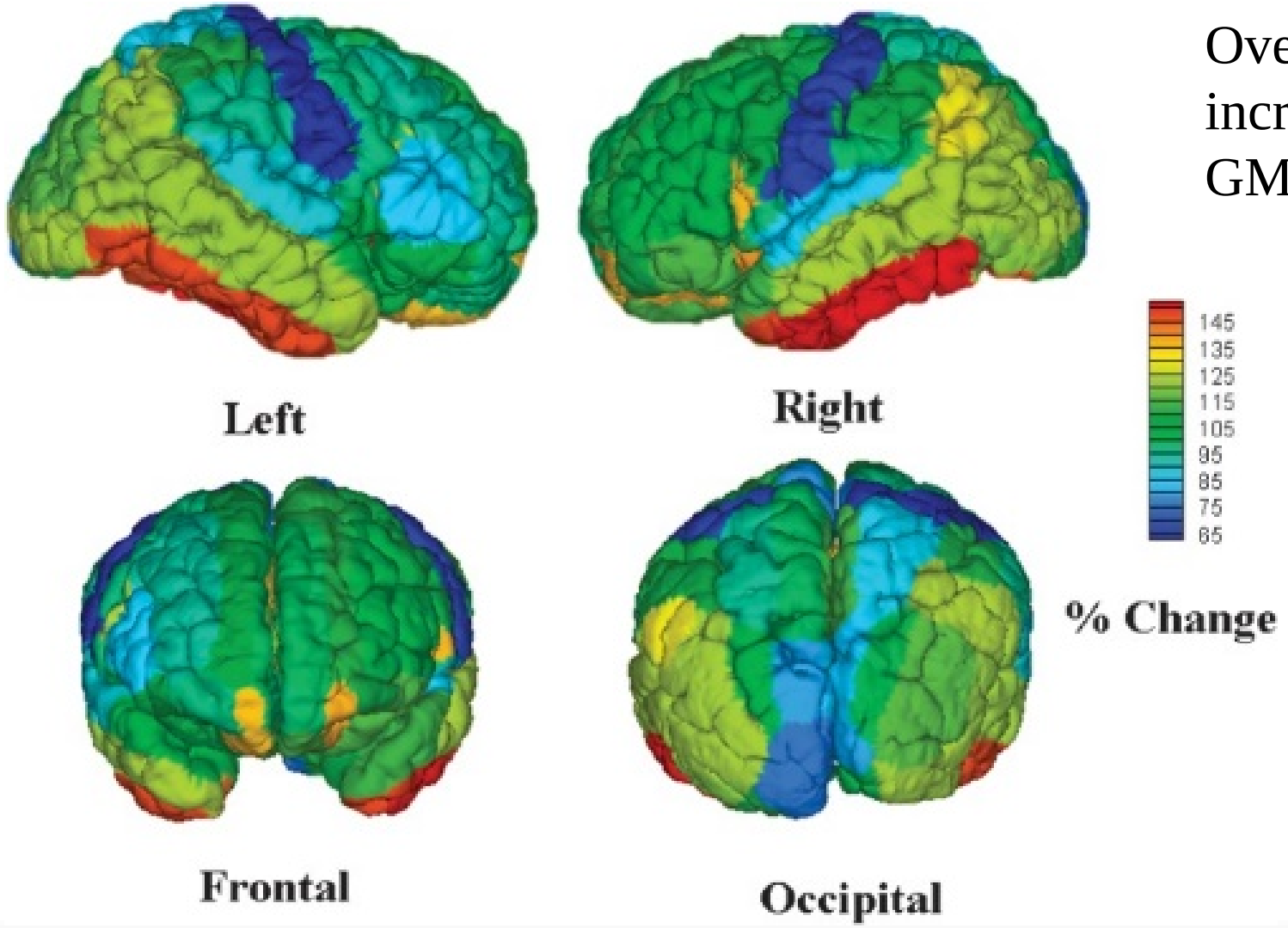
- The first two years of life involve rapid brain growth and development
- Brain development is ‘activity dependent’
- Critical periods for development

Typical brain development



Gilmore et al., 2012

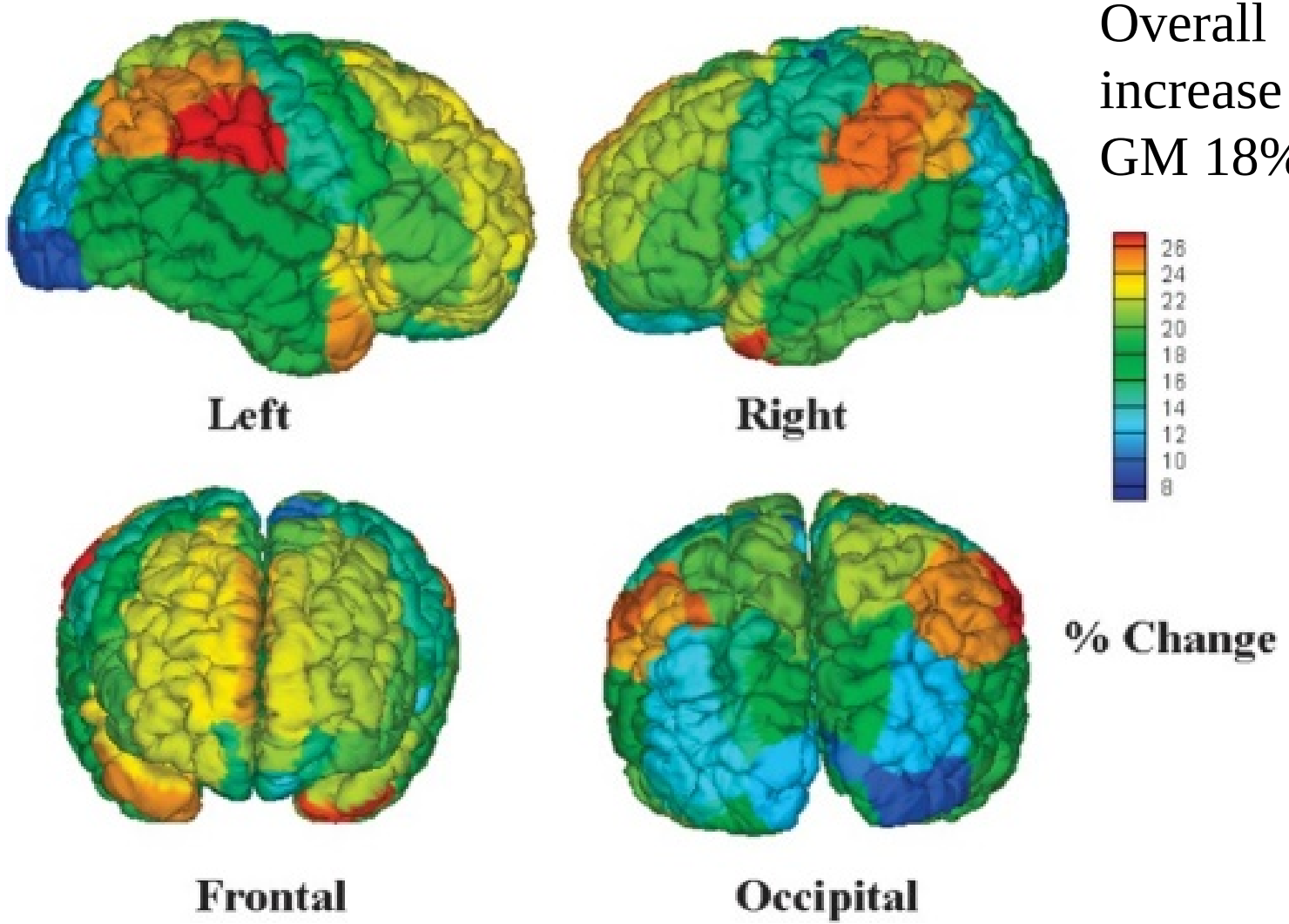
Gray matter maturation in 1st year



Overall increase in GM 106%

Gilmore et al., 2012

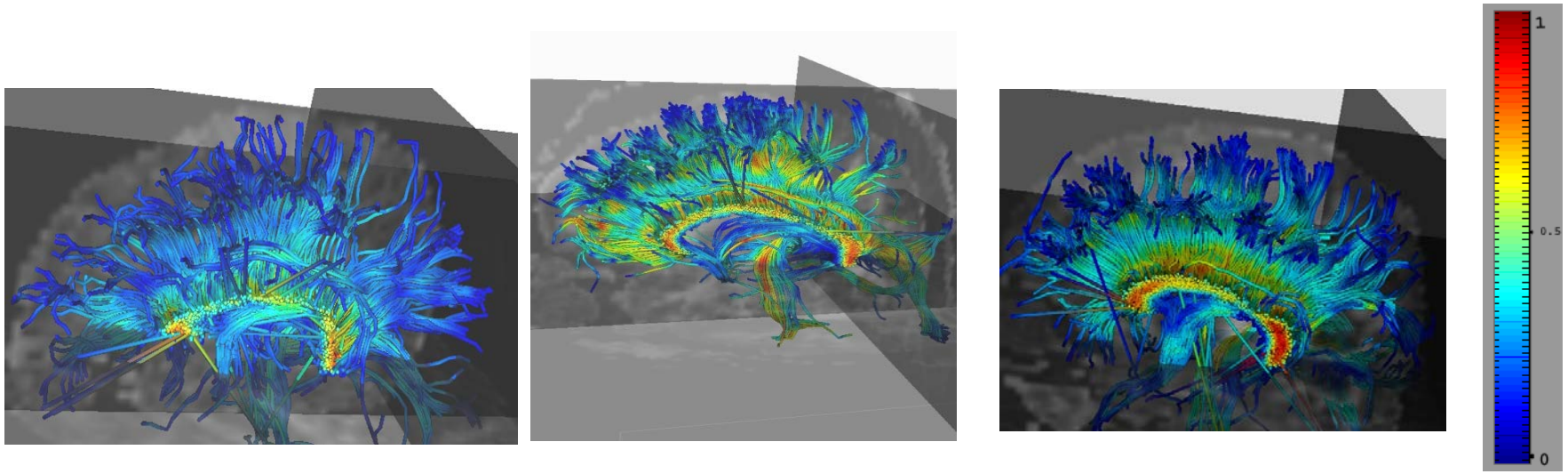
Gray matter maturation in 2nd year



Overall increase in GM 18%

Gilmore et al., 2012

White matter maturation



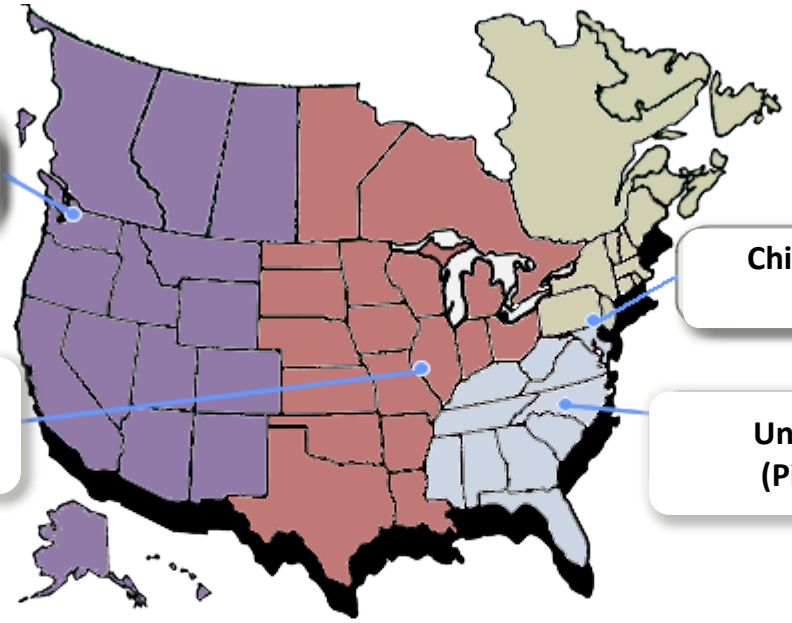
Neonate (2 wks) **Infant (1 year)** **Adult**

Corpus callosum: DTI (FA) along commissural bundles

Can brain differences be used to detect ASD?

IBIS (Infant Brain Imaging Study) Network

NIH Autism Center of Excellence (PI: Joseph Piven)



University of Washington
(Dager, Estes)

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Constantino)

University of North Carolina
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(Zwaigenbaum)

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New York University
(Gerig)

University of Minnesota
(Elison, Wolff)

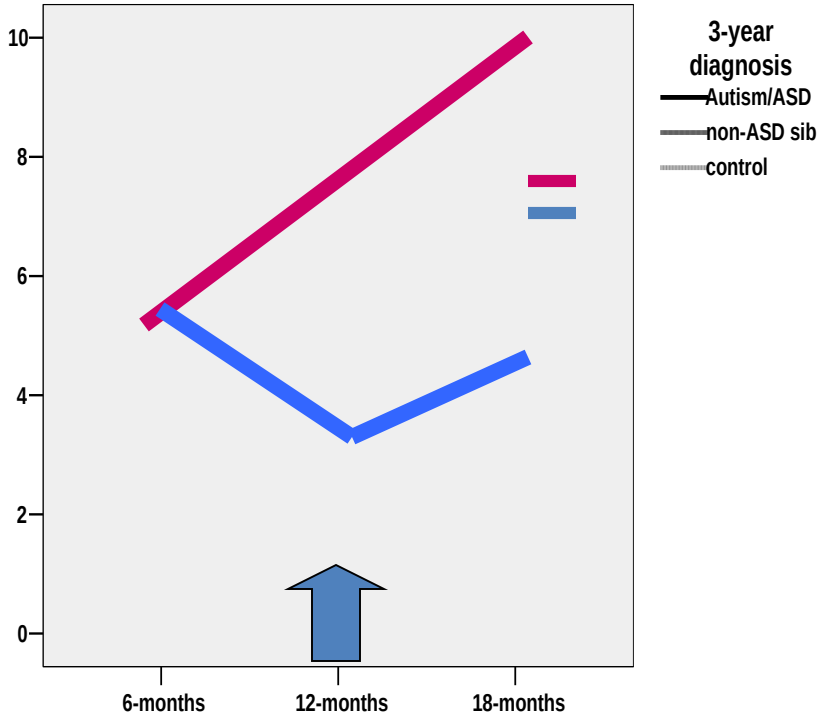
Johns Hopkins University
(Fallin, Volk)

Onset of Autistic Behavior and Brain Enlargement in the Latter Part of the First Year of Life

Onset of Autistic Behavior in At-Risk Infant Sibs Between 6-12 months

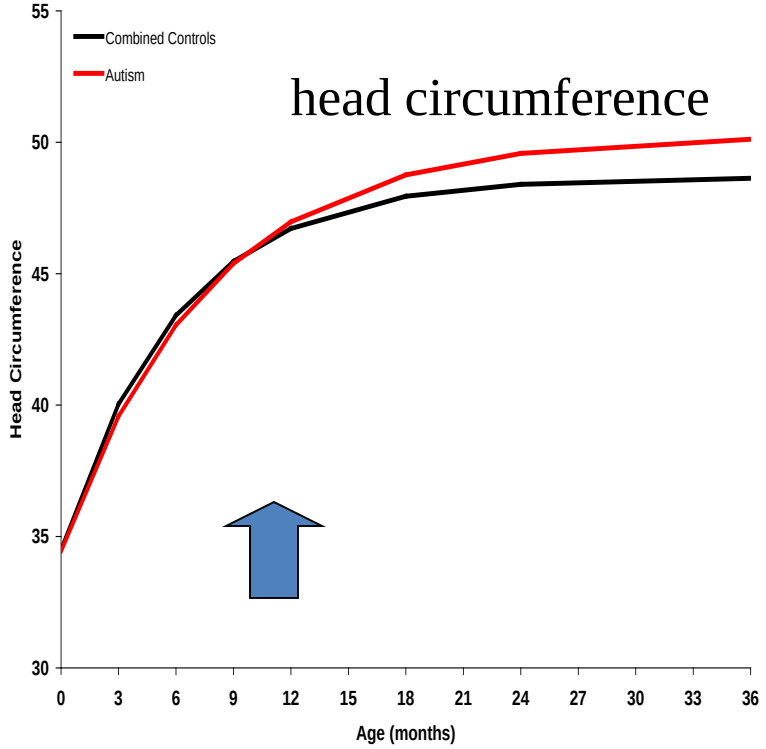
Onset of Brain Enlargement in Autistic Children before 12 mo.

Zwaigenbaum et al 2005



AOSI

Hazlett et al 2005



IBIS Network

- Infants at high-risk for autism (“baby sibs”) – younger sibling at increased risk (~20%)
- Seen longitudinally at 3, 6, 12, and 24 months with follow up at 36 m
- Developmental & behavioral assessments and MRI

LETTER RESEARCH

Nature 2017

Early brain development in infants at high risk for autism spectrum disorder

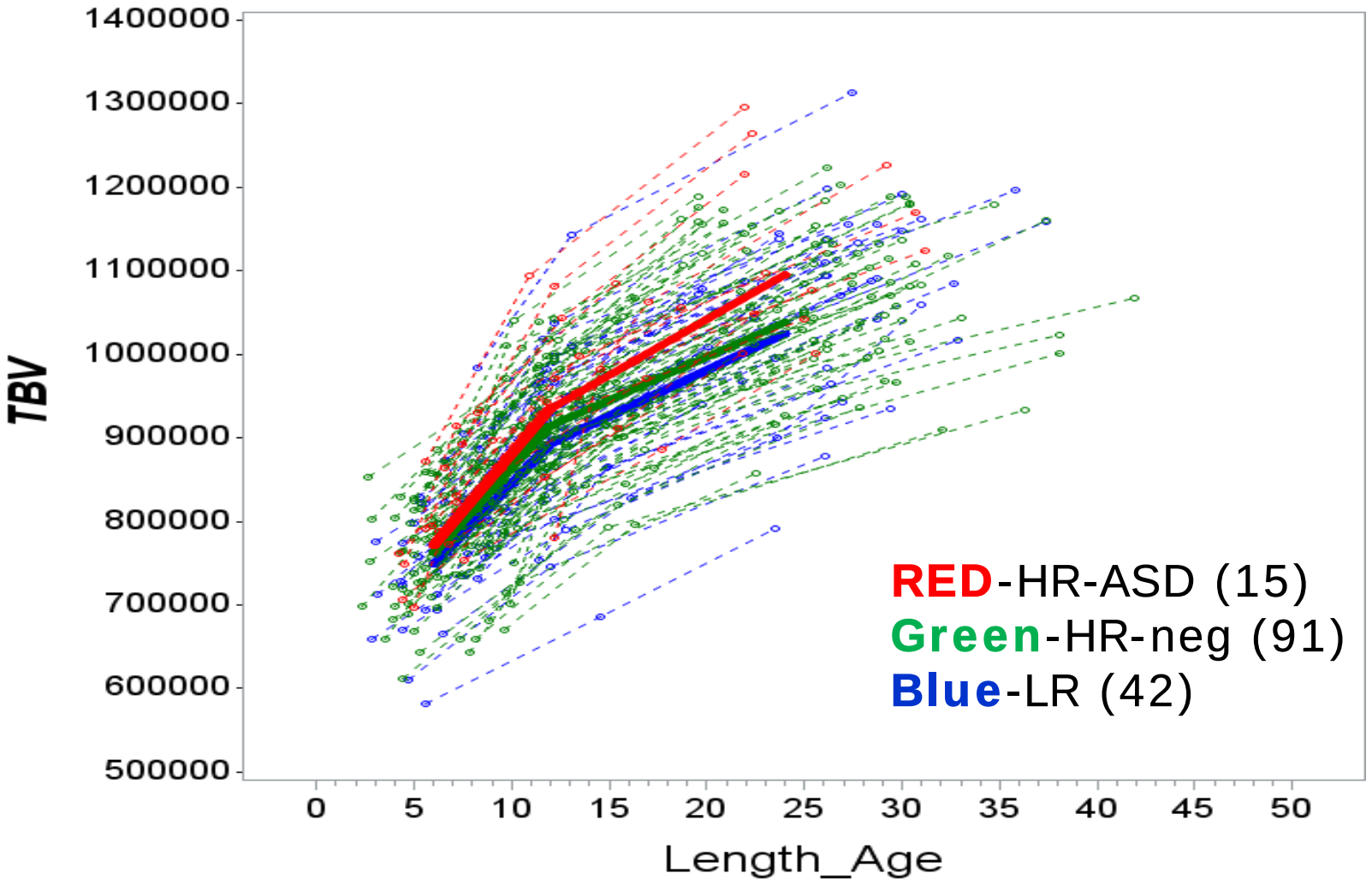
Heather Cody Hazlett[1,2], Hongbin Gu[1], Brent C. Munsell[3], Sun Hyung Kim[1], Martin Styner[1], Jason J. Wolff[4], Jed T. Elison[5], Meghan R. Swanson[2], Hongtu Zhu[6], Kelly N. Botteron[7,8], D. Louis Collins[11], John N. Constantino[7], Stephen R. Dager[8,9], Annette M. Estes[9,10], Alan C. Evans[11], Vladimir S. Fonov[11], Guido Gerig[12], Penelope Kostopoulos[11], Robert C. McKinstry[13], Juhi Pandey[14], Sarah Paterson[15], John R. Pruett Jr[7], Robert T. Schultz[14], Dennis W. Shaw[8,9], Lonnie Zwaigenbaum[16], Joseph Piven[1,2] & the IBIS Network*

Sample

	LR	HR-neg	HR-ASD	
N	117	248	70	
% males	59%	57%	83%	*
Maternal age (yrs)	33.2	33.2	33.3	
Birth weight (lbs)	8.0	7.9	7.9	
Gestational age (wks)	39.3	39.1	38.9	
Age at visit				
6m	6.7	6.6	6.6	
12m	12.7	12.7	12.7	
24m	24.6	24.7	24.6	
Mullen ELC at 24m	109.7	101.8	79.3	*
Vineland ABC at 24m	105.0	101.0	88.1	*

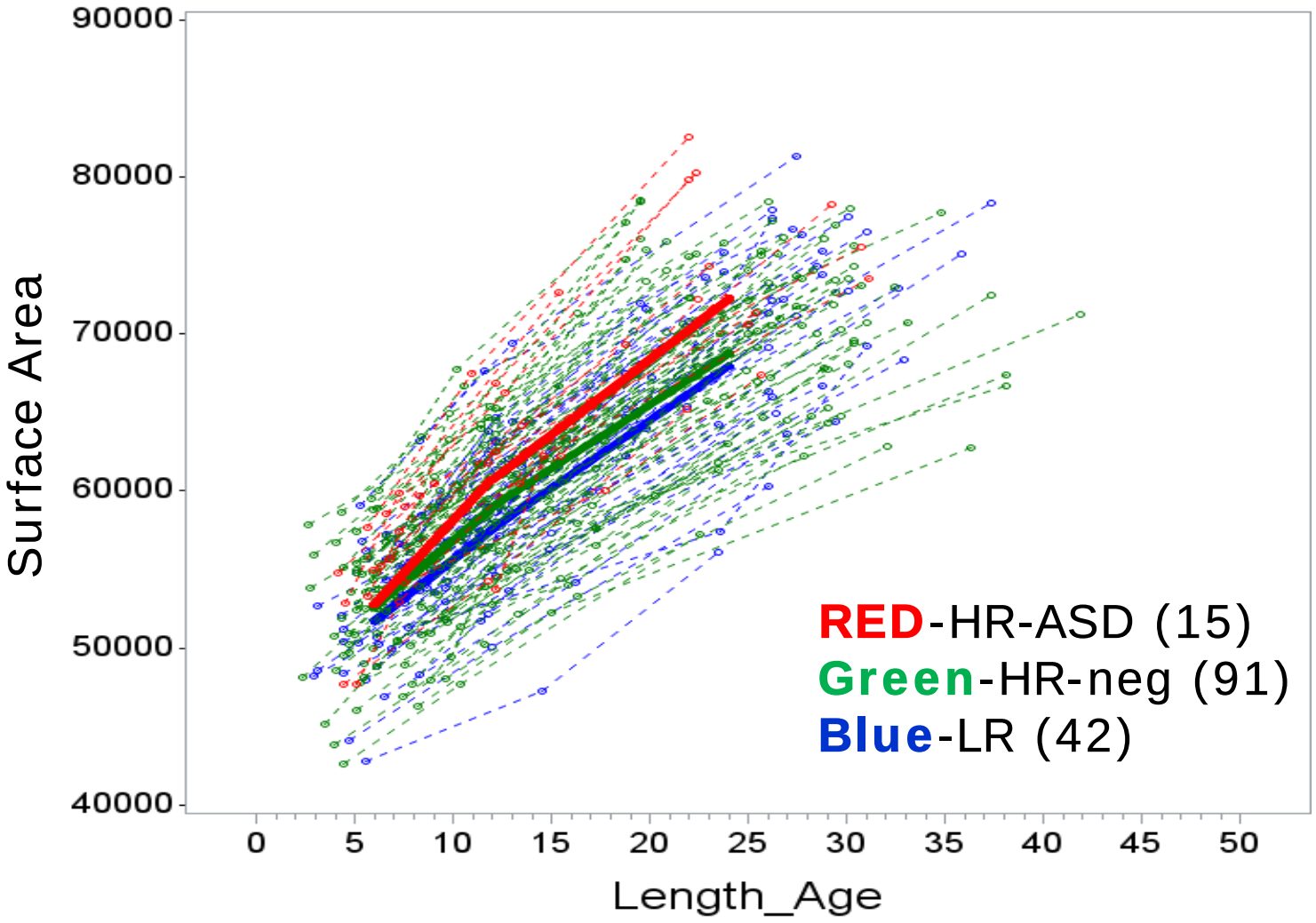
Note: also saw difference in maternal education

Brain overgrowth in HR-ASD



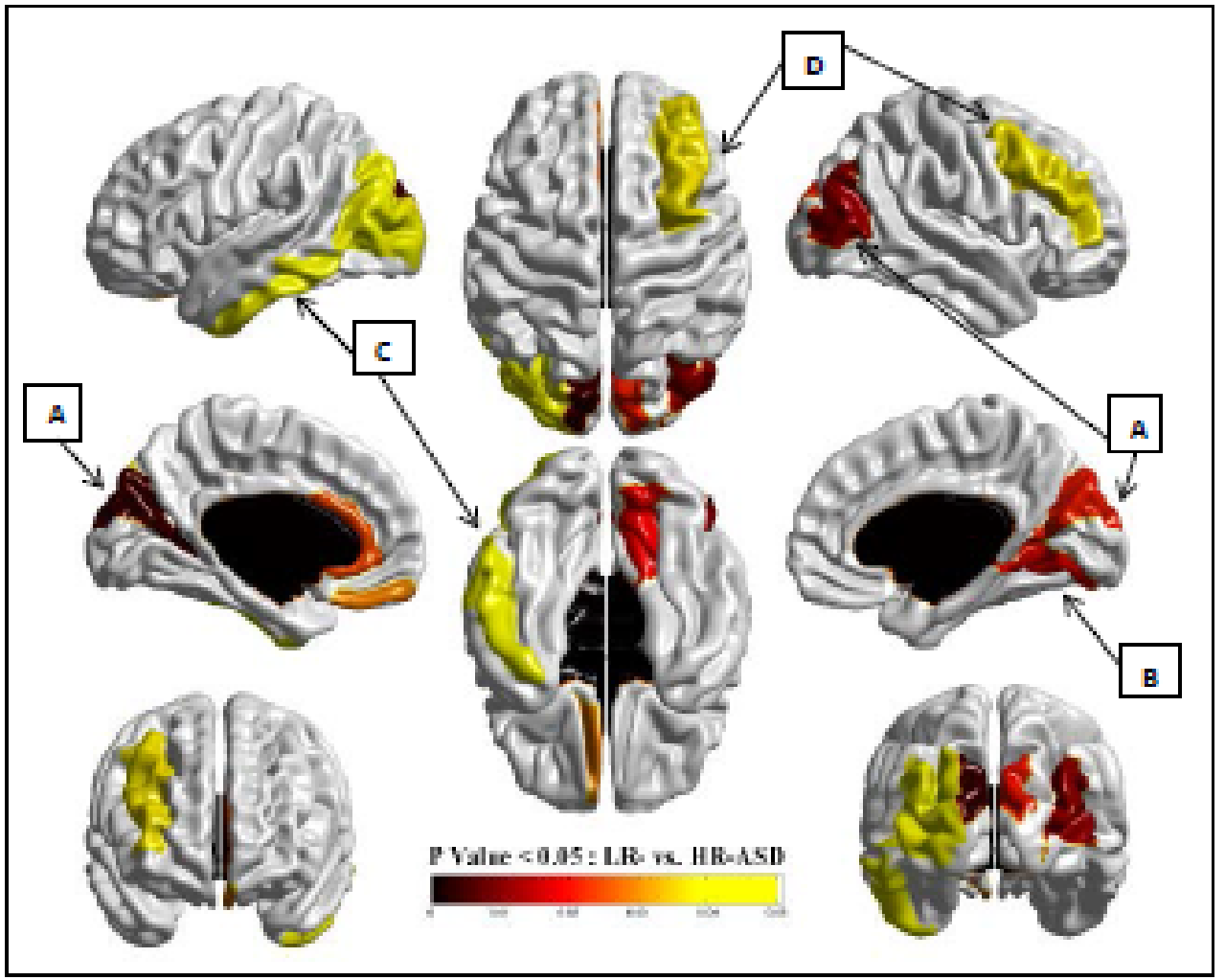
Hazlett et al., Nature 2017

Trajectory of surface area 6-24m



Hazlett et al., Nature 2017

Regions of SA expansion in HR-ASD



A=middle occipital gyrus & cuneus, B=lingual gyrus,
C=inferior temporal gyrus, D = middle frontal gyrus

Hazlett et al., Nature 2017

Brain enlargement associated with behavioral features

TBV growth rate & ADOS severity score

- no relationship at 6-12 month interval
- significant (positive) relationship at 12-24 months (p=0.06)
- relationship with social affect score, not repetitive behavior

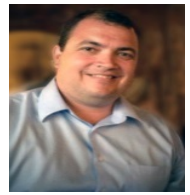
Relationship to social behaviors also seen in CSBS

- Social deficits at 24 months related to increased growth rate in TBV from 12-24 months

Could early surface area be a biomarker?

Deep Learning Classification of Cortical Data

Martin Styner, Ph.D. & **Brent Munsell, Ph.D.**
UNC **College of Charleston**



- predicting clinical best estimate diagnosis at 24 months:
  high risk–ASD versus high risk-negative
- 6 and 12 month scans
- cortical thickness & surface area; sex, total brain volume
- 78 ROI's x 2 hemispheres x 2 time points = 608 data points
- divide 179 (34 HR-ASD, 145 HR-neg) into 10 equal parts (folds) each with a HR-ASD/AR-Neg ratio ~ to total sample
- train on 9 parts/folds and test on 1 part/fold; average correct vs incorrect across all 10 folds

Hazlett et al., Nature 2017

Predicting 24 Month Diagnostic Outcome from 6-12 Month Surface Area

	ASD (n=34)	Non-ASD (n=145)	
Positive Test (ASD)	True Positive (TP) N=30	False Positive (FP) N=7	**PPV = 81%** **TP/(TP + FP)**
Negative Test (Non-ASD)	False Negative (FN) N=4	True Negative (TN) N=138	**NPV = 97%** **TN/(FN + TN)**
	Total ASD	Total non-ASD	
	sensitivity = 88% **TP/ASD**	**specificity = 95%** **TN/non-ASD**	

features correctly classify ~ 8 of 10 (81%) of infants as ASD

Predicting Later Autism from Early Behavior?

Article

autism

Autism
17(5) 527–540

DOI: 10.1177/1362361312439633
aut.sagepub.com
SAGE

The First Year Inventory: a longitudinal follow-up of 12-month-old to 3-year-old children

Autism; 2013

Lauren M Turner-Brown
University of North Carolina at Chapel Hill, USA

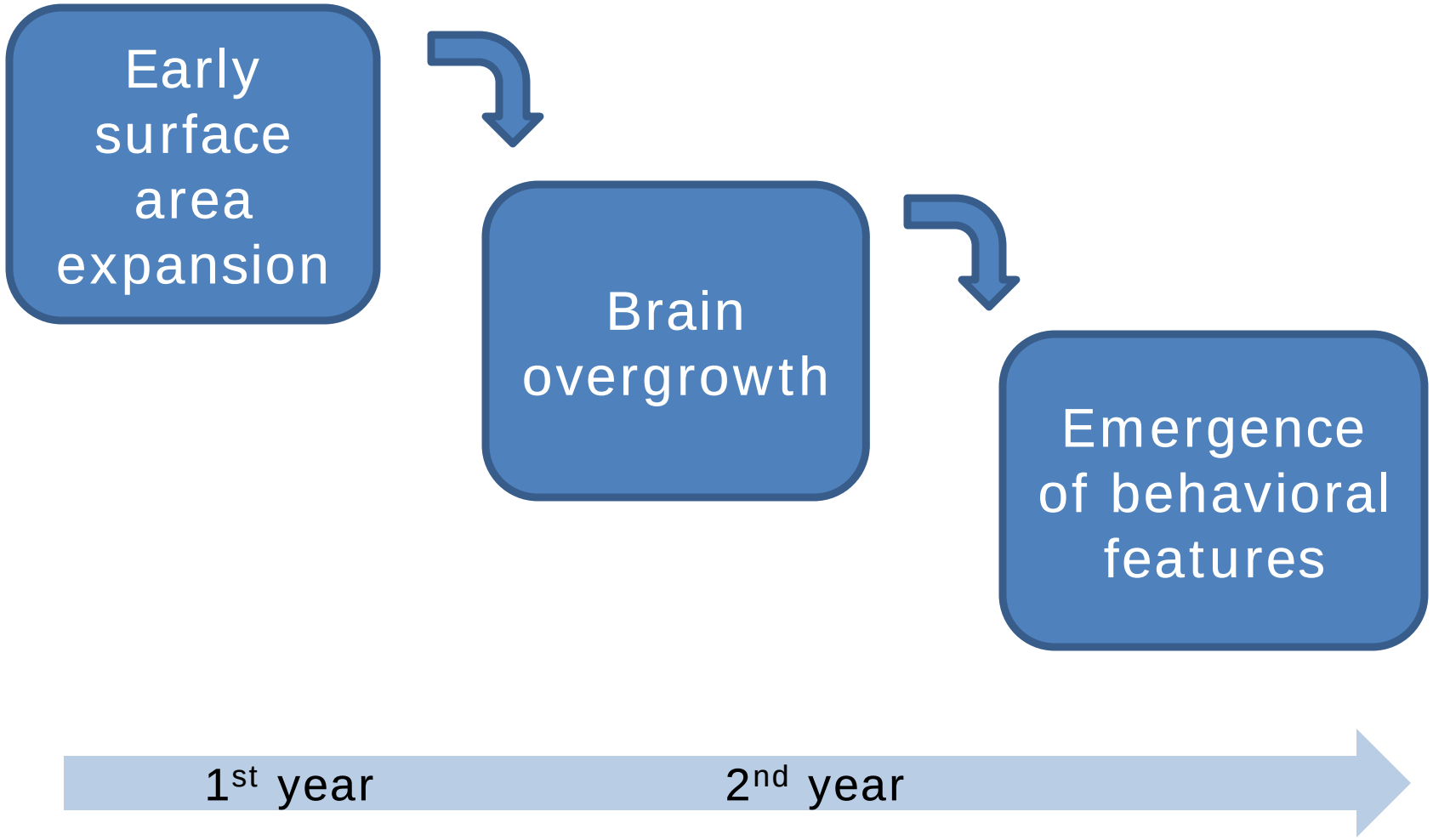
PPV = .14
no validation sample

18-Month Predictors of Later Outcomes in Younger Siblings of Children With Autism Spectrum Disorder: A Baby Siblings Research Consortium Study

JAACAP 2014

Katarzyna Chawarska, PhD, Frederick Shic, PhD, Suzanne Macari, PhD, Daniel J. Campbell, PhD, Jessica Brian, PhD, Rebecca Landa, PhD, Ted Hutman, PhD, Charles A. Nelson, PhD, Sally Ozonoff, PhD, Helen Tager-Flusberg, PhD, Gregory S. Young, PhD, Lonnie Zwaigenbaum, MD, Ira L. Cohen, PhD, Tony Charman, PhD, Daniel S. Messinger, PhD, Ami Klin, PhD, Scott Johnson, PhD, Susan Bryson, PhD

PPV = .50
in a validation sample


Early surface area expansion
Brain overgrowth
Emergence of behavioral features
1st year
2nd year

Summary of findings

brain changes are present as early as **6 months of age** (before the appearance of the defining features of autism)

the brain in autism **changes over time** (age 6 – 24 months) … during a critical period when autistic behavior is first unfolding

Clues to mechanisms?

Neocortical neurogenesis and the etiology of autism spectrum disorder (2016). Alan Packer (SFARI)

Some ASD risk genes have role in neurodevelopment

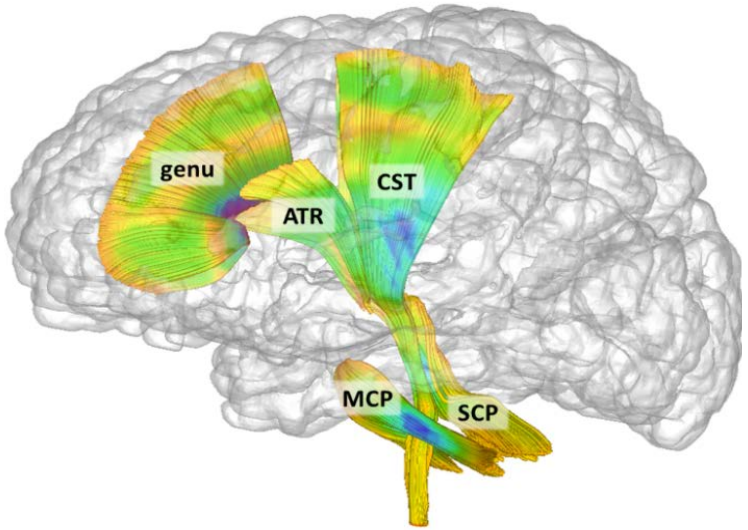
Altered neurogenesis?

Neural progenitor cell proliferation?

Other evidence for early brain differences and ASD outcomes?

Neural circuitry at age 6 months associated with later repetitive behavior and sensory features in autism

JasonWolff



ATR = anterior thalamic radiation; **CST** = cortico-spinal tract; **genu** = genu of corpus callosum; **MCP** = mid-cerebellar peduncle; **SCP** = superior cerebellar peduncle

HR-ASD (N=44); **HR-NEG** (N=173)

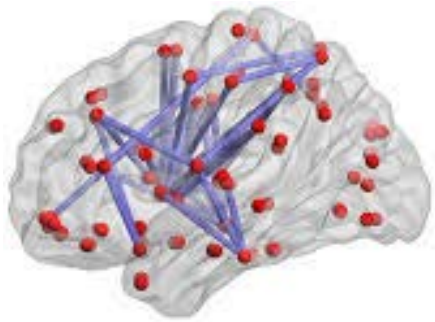
- DTI tracts at 6, 12 and 24 months
- Behavior: RBS-R, SEQ

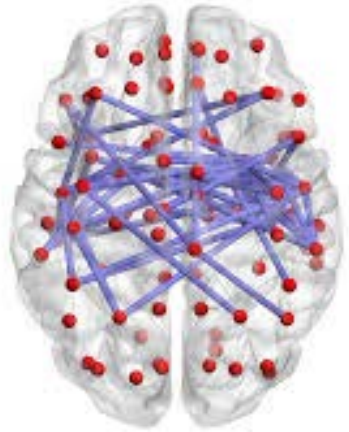
Genu FA & Cerebellar pathways at 6 months → Repetitive behavior & sensory features at 24 months

- **no association** between genu/cerebellar tracts and ADOS **social affect** score

Wolff et al, Mol Autism 2017

Examining brain networks





6 Months of Age

functional connectivity networks from rsMRI

Robert Emerson

Using functional connectivity at 6 months to predict ASD outcomes at 24 months

Future directions and next steps

- Explore brain-behavior relationships in cortical and subcortical data
- Multi-modal analyses (e.g, sMRI, DTI, bx)
- Individual profiles and domain based trajectories (e.g., RDoC)
- Incorporate genetics and environmental risk data

Infant Brain Imaging Study (IBIS) NIH ACE Network

University of North Carolina
Joe Piven
Heather Cody Hazlett
Martin Styner
Hongbin Gu
Chad Chappell

Children's Hospital of Philadelphia
Robert Schultz
Juhi Pandey
Ragini Verma
Sarah Paterson (Temple)

NY University
Guido Gerig

University of Washington
Stephen Dager
Annette Estes

University of Alberta
Lonnie Zwaigenbaum

McGill University
Alan Evans
Louis Collins
John Lewis
Samir Das
Leigh MacIntyre
Penelope Kostopoulos

Washington University in St Louis
Kelly Botteron
John Constantino
Bob McKinstry
John Pruett

University of Minnesota
Jed Elison
Jason Wolff

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Many thanks to the participating families!

Meeting of the IACC

Afternoon Agenda - continued

2:30 Extra-Axial Cerebrospinal Fluid as a Potential Biomarker in Infants Who Develop ASD and Insights into the Role of Early Behavior

Mark Shen, Ph.D.
Postdoctoral Fellow
Carolina Institute for Developmental Disabilities
University of North Carolina School of Medicine

Extra-Axial Cerebrospinal Fluid as a Potential Biomarker in Infants Who Develop ASD and Insights into the Role of Early Behavior

Mark Shen, PhD

Postdoctoral Fellow

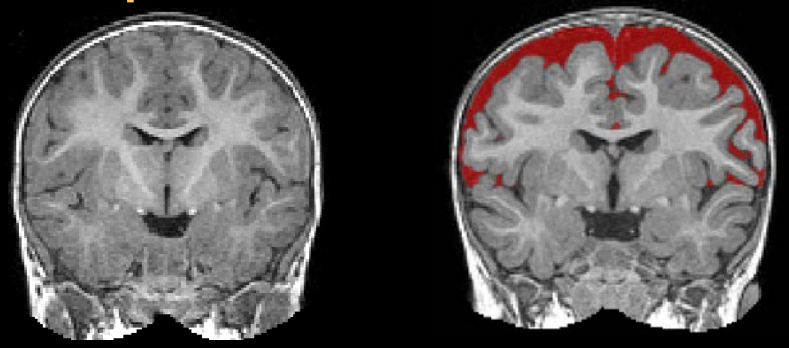
University of North Carolina

mark_shen@med.unc.edu

UNC CAROLINA INSTITUTE FOR DEVELOPMENTAL DISABILITIES

IACC Meeting
April 26, 2017

Initial Report of Extra-Axial CSF



- 2013: Published ini1al finding at UC Davis MIND Ins1tute

BRAIN
A JOURNAL OF NEUROLOGY

Early brain enlargement and elevated extra-axial fluid in infants who develop autism spectrum disorder

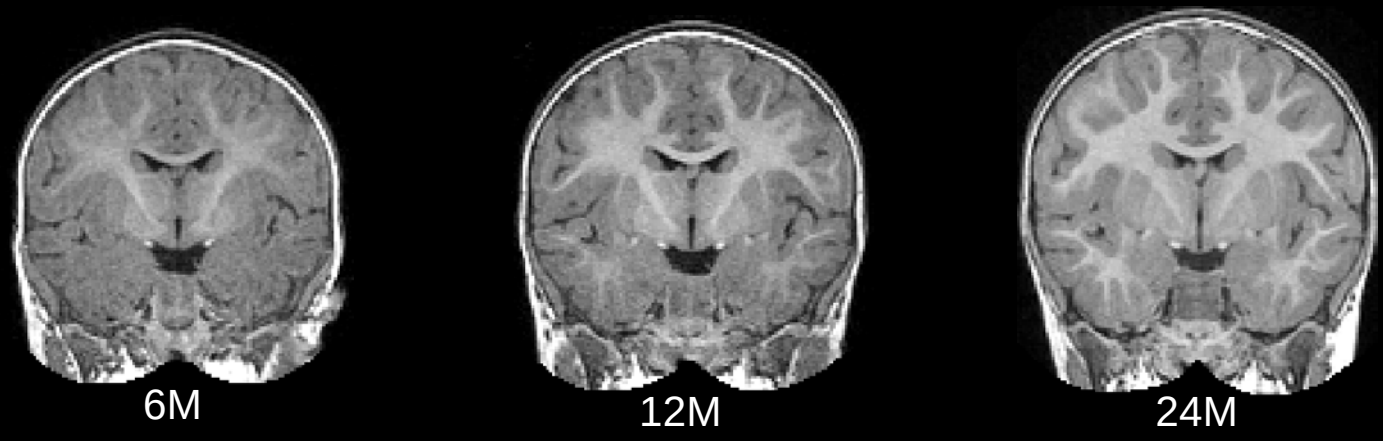
Mark D. Shen,[1] Christine W. Nordahl,[1] Gregory S. Young,[1] Sandra L. Wootton-Gorges,[2] Aaron Lee,[1] Sarah E. Liston,[1] Kayla R. Harrington,[1] Sally Ozonoff[1] and David G. Amaral[1]

- Total sample: **N=55 (ASD=10)**

Shen et al., 2013

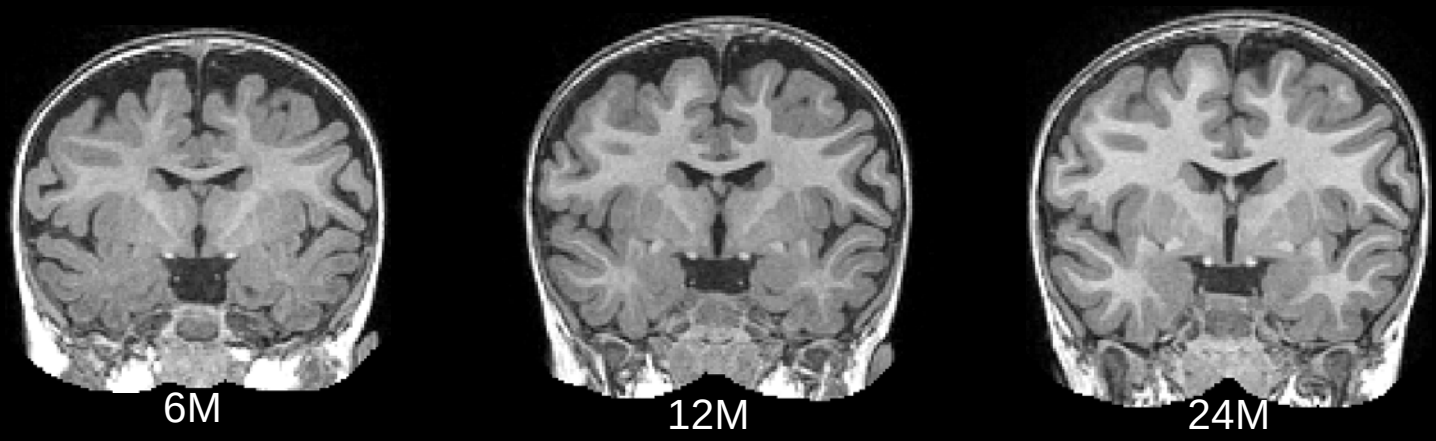
Extra-Axial CSF from 6-24 months

Low-Risk Infant with Normal MRI; ASD-negative



6M 12M 24M

High-Risk Infant with Increased Extra-Axial CSF; Diagnosed with ASD



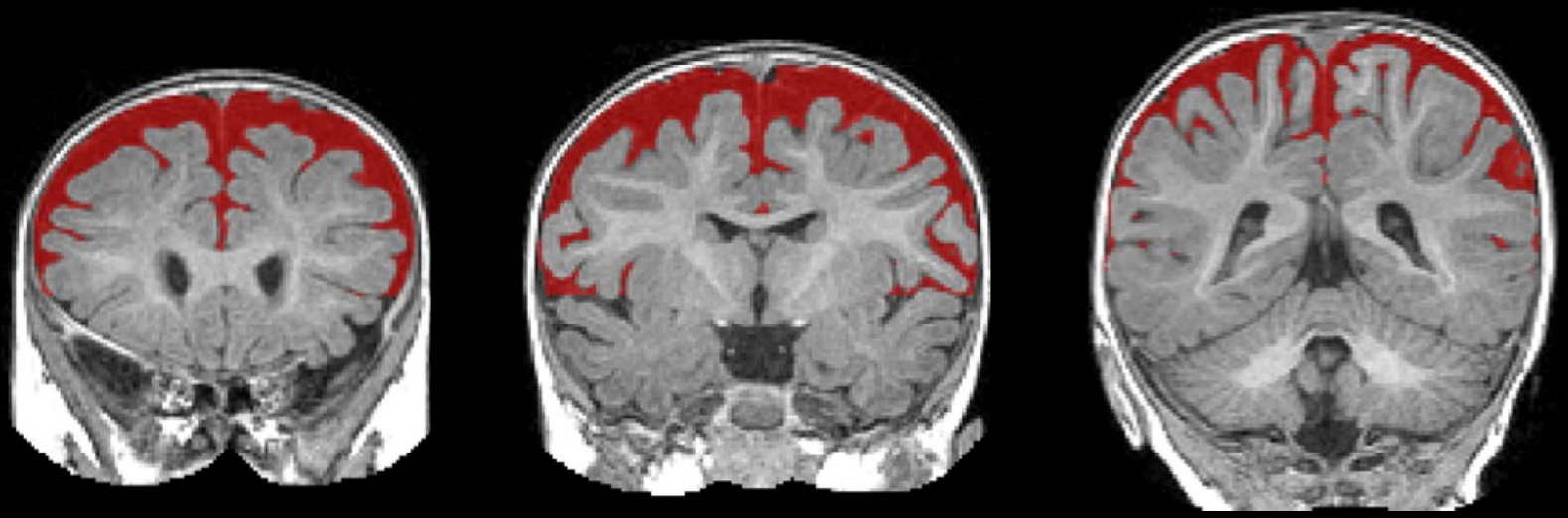
6M 12M 24M

(Shen et al., 2013, Brain)

Infant Brain Imaging Study (IBIS) Network

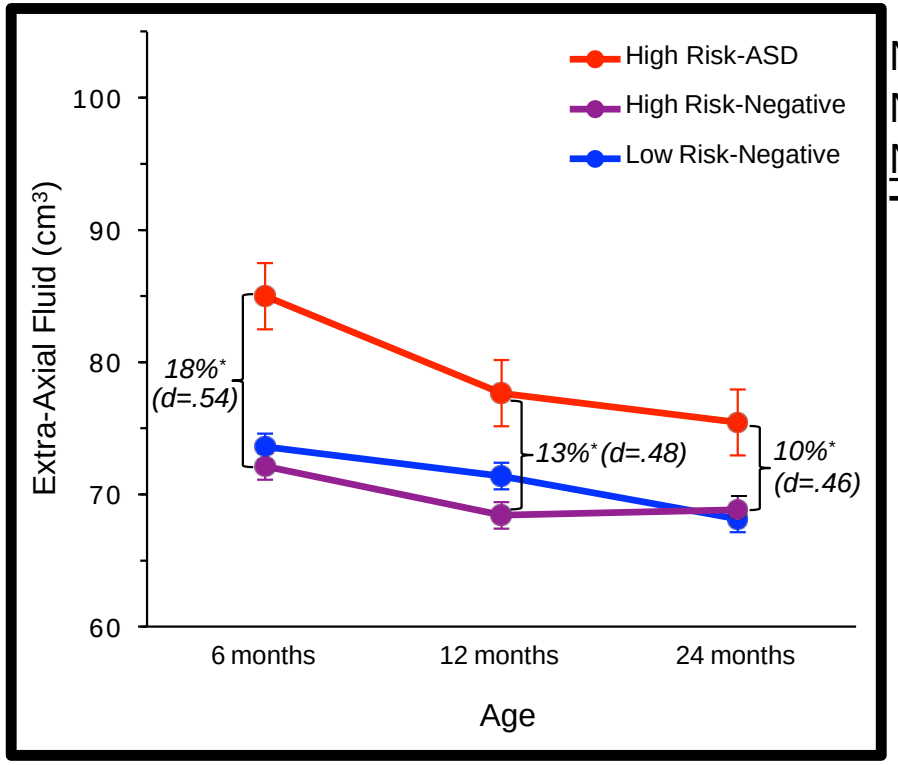
- MRI Scans at 6, 12, 24 months; Diagnosis at 24M
- 4 clinical data collec1on sites
- **N=343 infants** (804 total scans)

Automatic Segmentation of Extra-Axial CSF:



(Shen et al., 2017, Biol Psych)

HR infants later diagnosed with ASD had increased Extra-Axial CSF by 6 months, persistently elevated through 24 months



N=47
N=174
N=122
Tot = 343

%diff vs. HR-negaBve (Cohen's d effect size)

Covariates: Age, Sex, Site, Total Cerebral Volume

**p<0.005 vs. LR-neg, HR-neg*

(Shen et al., 2017, Biol Psych)

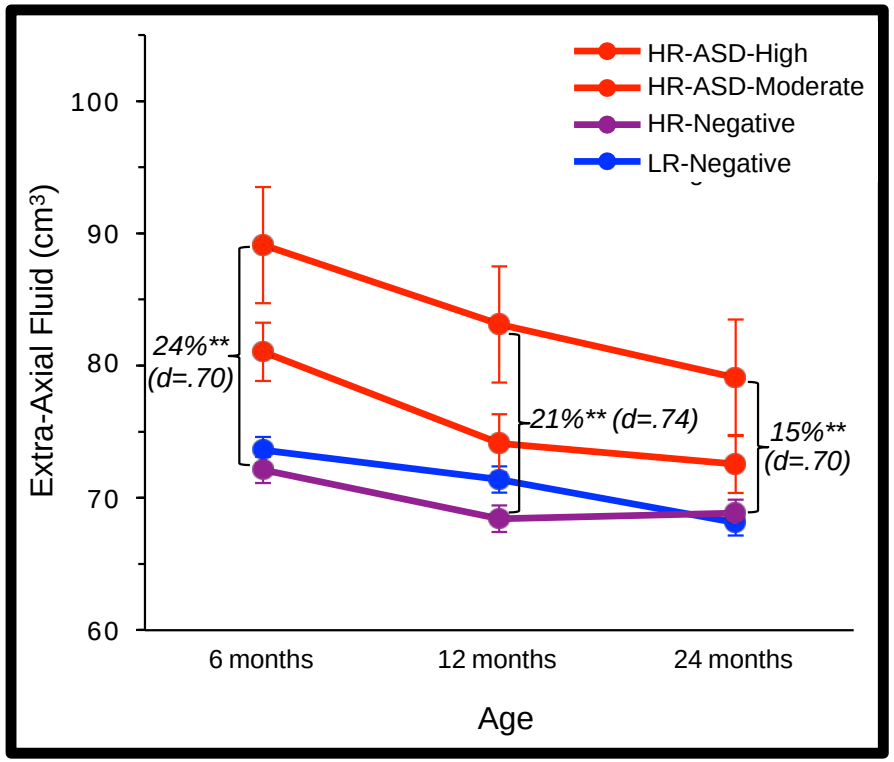
Large ASD group (n=47)

…

Examine subgroups based on symptom severity

(Gotham & Lord, 2007)

More pronounced increase of Extra-axial CSF in more severe ASD subgroup



N=23
N=24
N=174
N=122
Tot = 343

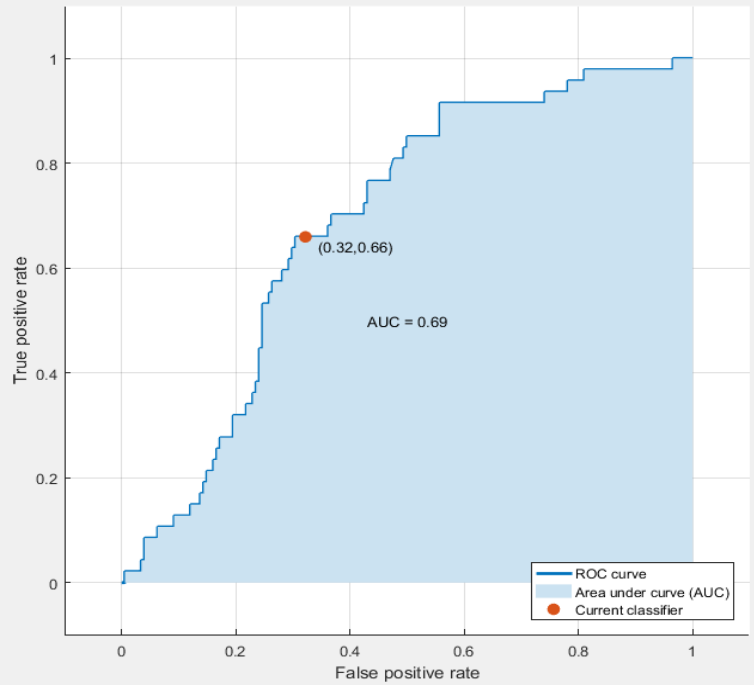
Covariates: Age, Sex, Site, Total Cerebral Volume

***p<0.05 vs. all other groups*

(Shen et al., 2017, Biol Psych)

Extra-axial CSF as a single brain measure at 6 months has modest prediction accuracy of ASD diagnosis at 24 months

25-fold cross-validation
Logistic regression (ROC curve)



IBIS 2017 sample:
- Overall accuracy =69%
- Sensitivity at 6 months = 66%
- Specificity at 6 months = 68%

Externally validated in MIND 2013 sample:
- Overall accuracy = 72%
- Sensitivity at 6 months = 80%
- Specificity at 6 months = 67%

1. Observable, reliable brain anomaly
2. Detectable w/ any structural MRI
3. Replication is rare

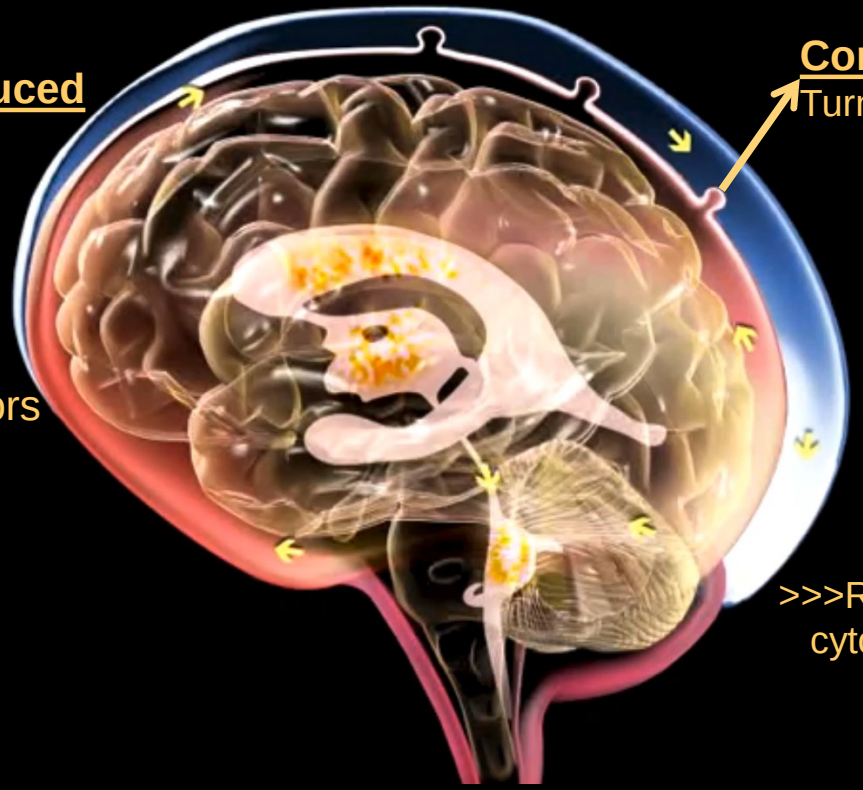
(Shen et al., 2017, Biol Psych)

CSF: Filtration System of Brain

Xie, 2013 (Science)
Iliff, 2012 (Science Transl Med)
Louveau, 2015 (Nature)

Continuously produced

Delivers growth factors
>>>developing brain



Continuously absorbed
Turns over every 6 hours

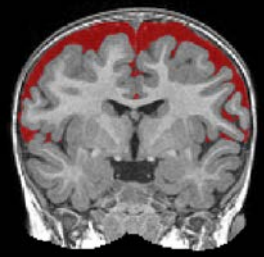
>>>Removes inflammatory cytokines, metabolites (Aβ)

Neuroinflammation?

Cytokine accumulation?

4/26/2017
video: medical-animations.com

Current follow-up studies
(unpublished)



1) ***What is the specificity?***
   - Is it present in monogenic subtypes of ASD?
     Or in other neurodevelopmental disorders?

2) ***What is the pathogenic mechanism?***
   - **Using mouse models to test hypothesized mechanism of neuroinflammation**

3) ***Are there genetic variants associated with extra-axial CSF?***
   - DNA in family quads (infant, parents, older ASD sibling)
   - Genome-wide SNP genotyping, Whole-exome sequencing, Polygenic risk scores

4) ***Combined with other brain/behavioral measures to improve prediction?***

(Collaborators: David Amaral, Joseph Buxbaum, Dani Fallin, Patrick Sullivan, John Gilmore, Ben Philpot)

Integrating behavior & early language environment

(Meghan Swanson et al., 2017)

Brain development doesn't occur in avacuum

LENArecorder = "Language Pedometer"

-Whole-day recordings @ 9 months
-NaturalisBc, home environment

Automated detection of “Hyper-vocalizers”

CHILD DEVELOPMENT

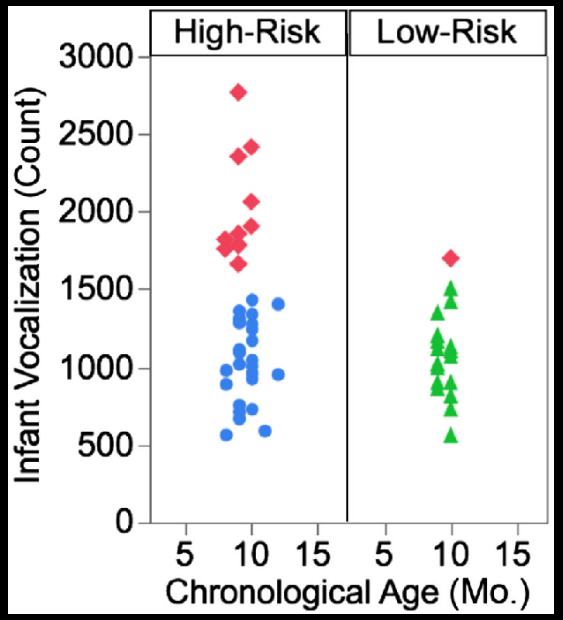
Child Development, xxxx 2017, Volume 00, Number 0, Pages 1–14

Naturalistic Language Recordings Reveal “Hypervocal” Infants at High Familial Risk for Autism

Meghan R. Swanson

University of North Carolina at Chapel Hill

Meghan Swanson
Postdoc (K99/R00)



- **20% of HR infants were “hyper-vocal” at 9 mos.**
  - Parents of high- and low-risk infants provided equally rich language environments
- Hyper-vocalizers had lower social babbling (AOSI)
  - **Early stereotyped behavior?**
- **To be continued… 24 month diagnosis?**

Example of the added value of behavior:

Hyper-vocalizaBon as an early marker for heterogeneous outcomes?

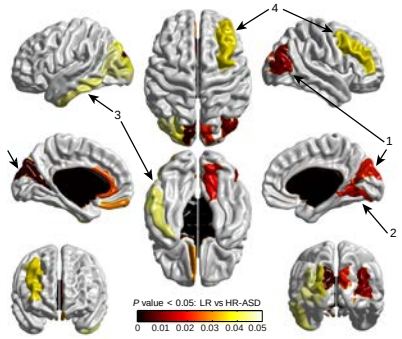
Meghan Swanson
Postdoc (K99/R00)

- Moving beyond dichotomous outcomes (ASD, not ASD) to understanding an early trajectory of heterogeneous outcomes
  - More/less social, language delay

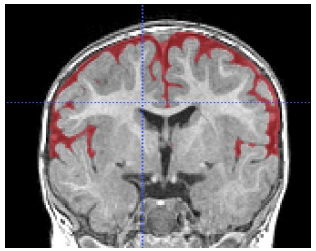
- Benefits:
- Scalable, high-throughput, quantifiable, and objective
  - Attributes that are critical for a potential early marker

- Cost-effective:
  - Easily implemented by sending recorders in mail
  - Data is automated

Mul1-dimensional Approach to Early Markers of Au1sm

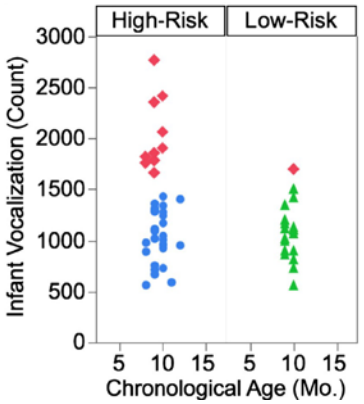


Brain surface area/volume:
increased proliferaBon of progenitor cells

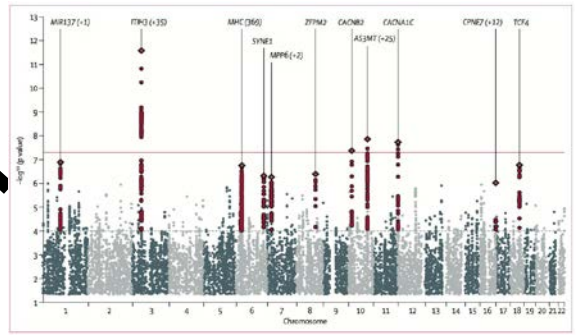


Extra-axial CSF
AccumulaBon of inflammatory cytokines

1. Improve predicCon in infancy
2. Develop personalized treatments



Early language/ psychological environment



Molecular gene1cs

Mark Shen (mark_shen@med.unc.edu).

~Thank you to all of the families and children who participated in the study~

IBIS Network

University of North Carolina
- Joe Piven
- Heather HazleN
- MarCn Styner
- Meghan Swanson
- Sun Hyung Kim
- Hongbin Gu
- Robert Emerson
- Rachel Smith
- Mike Graves
- Chad Chappell

University of Washington
- AnneNe Estes
- Dennis Shaw
- Stephen Dager

Washington University
- Kelly BoNeron
- John ConstanCno
- Bob McKinstry
- John PrueN

CHOP
- Robert Schultz
- Sarah Paterson
- Juhi Pandey

University of Alberta
- Lonnie Zwaigenbaum

University of Minnesota
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NYU
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- Clement Vachet

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Au1sm Speaks
Simons Founda1on

UC Davis MIND Ins1tute:
David Amaral
Chris1ne Nordahl
Sally Ozonoff
Sally Rogers
Greg Young

Gene1cs:
Dani Fallin
Joseph Buxbaum
Patrick Sullivan

LENA:
Mark Clements
James Rehg

Mouse models:
Ben Philpot
Bin Gu
M a i Judson
Sheryl Moy

Joseph Buxbaum
Ting Wang
Carla Golden
Hala Harony

Schizophrenia:
John Gilmore
Rebecca Knickmeyer

4/26/2017

Mark Shen (mark_shen@med.unc.edu).

Meeting of the IACC

Afternoon Agenda - continued

2:45 Digital Clinical Assessment for Diagnosis and Treatment Outcome Measurement

Robert Schultz, Ph.D.
RAC Professor of Psychology
Departments of Pediatrics and Psychiatry
Director of the Center for Autism Research
University of Pennsylvania

3:00 Panel Discussion

3:30 Afternoon Break

Digital Clinical Assessment for Diagnosis and Treatment Outcome Measurement

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University of Pennsylvania

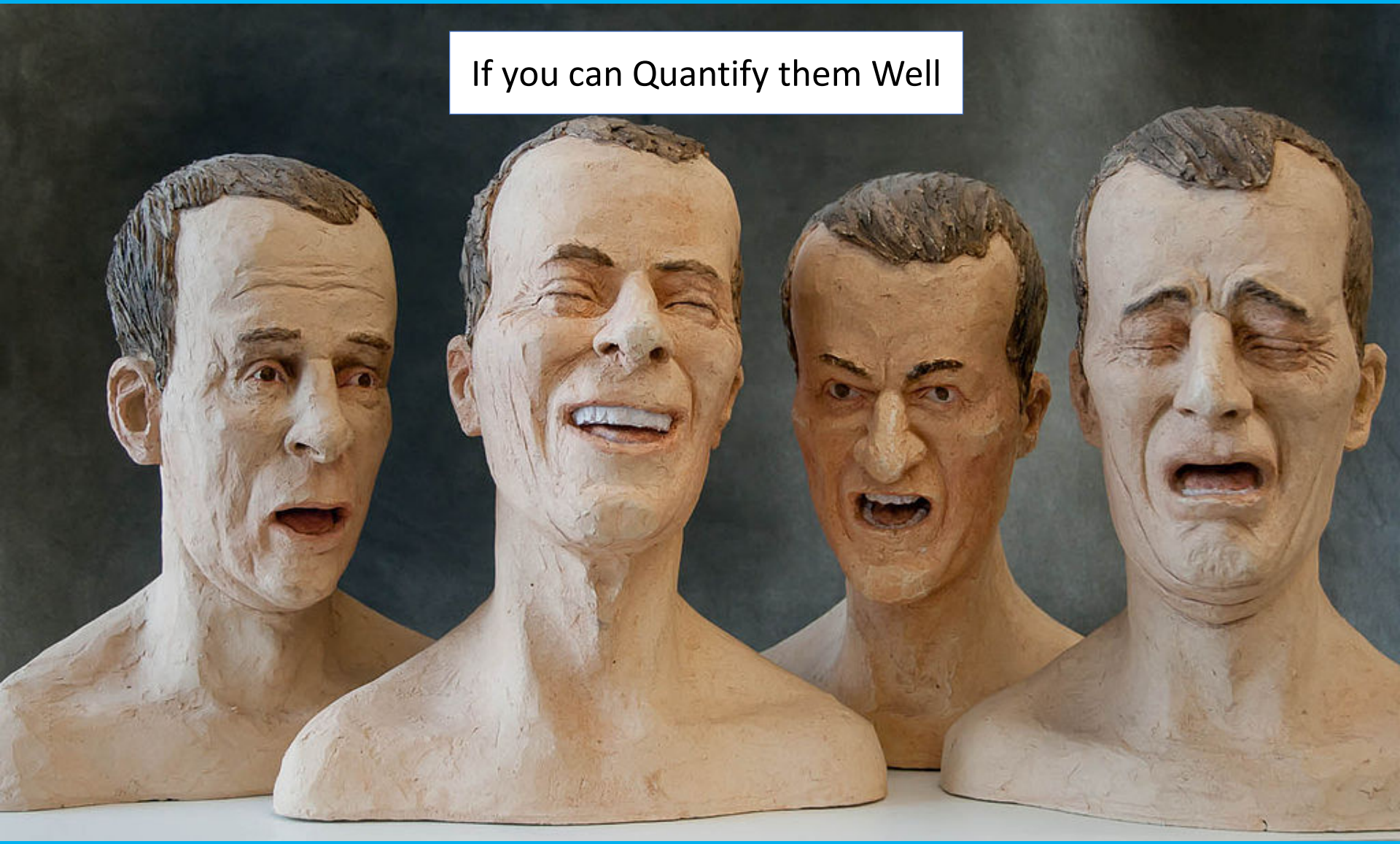
Digital Assessment for Diagnosis & Treatment Outcome Measurement

Bob Schultz, PhD

Director, Center for Autism Research
Children's Hospital of Philadelphia
RAC Endowed Professor, Depts. of Pediatrics & Psychiatry
Perelman School of Medicine
University of Pennsylvania

No disclosures related to this research

Behaviors are exquisitely organized representations of neural circuitry activity, i.e. Biomarkers



Autism is a Behaviorally Defined Condition

Perceptual Computing:

All behaviors observable by an autism expert can be digitally captured and analyzed to make predictions (e.g. diagnosis, treatment response, biological substrate)

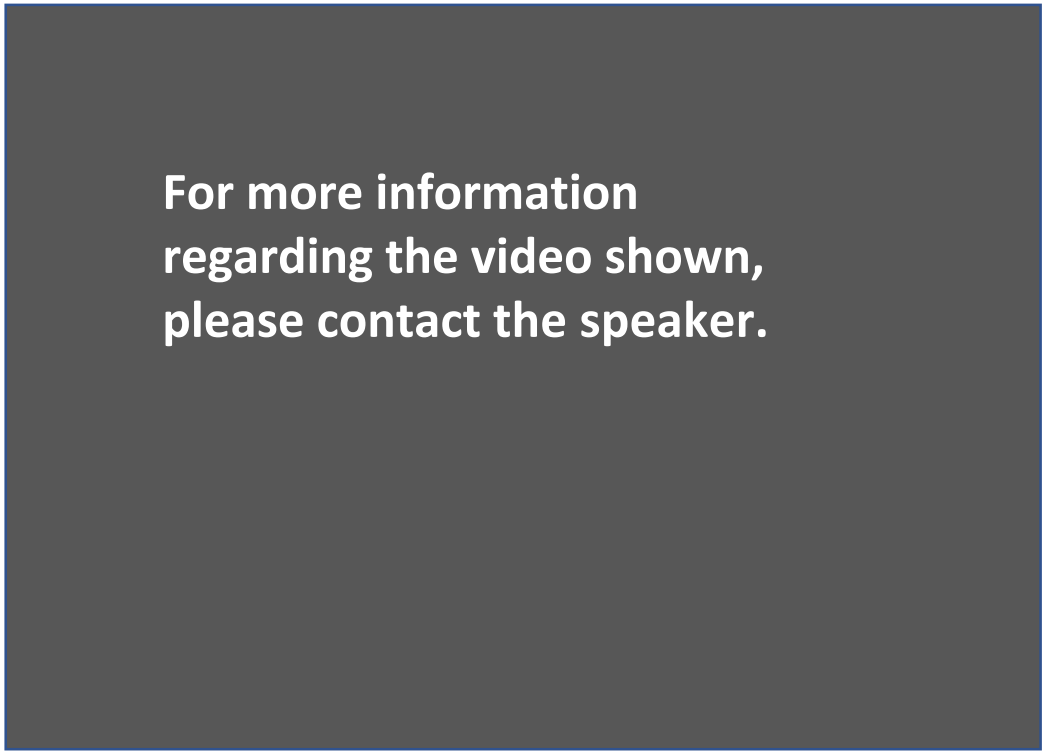
- In the lab, as well as natural everyday contexts
- Perfect attention and memory

These can all be digitally captured with very high accuracy

- Repetitive Behaviors, Imitation: Gross Motor
- Facial expression, gesture, eye contact: Nonverbal Communication
- Acoustic properties of speech – rate, volume, prosody
- Language (reflects inner life, restricted interests)
- Autonomic nervous system activity (anxiety, arousal)

- For **Precise Measurement & Prediction**
  - dx, granular characterization, intervention planning for core and other features of ASD (or any condition), intervention response, side effect monitoring, natural history description, genetic variants, brain imaging …

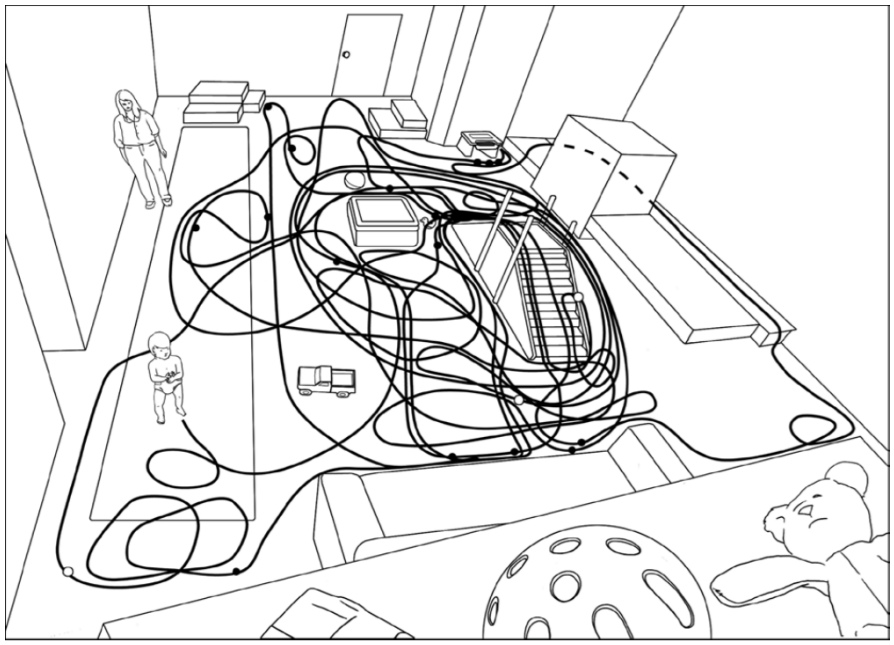
Measuring Gross Motor Behavior



- **Motor Coordination**
- **Balance/Postural stability**
- **Repetitive Behaviors, Stereotypies**

Gross Motor delay one of the earliest signs of autism risk

Exploration, Social Approach, Motor Learning



Adolph et al. 2012. Learning to walk. Thousands of Steps and Dozens of Falls Per Day

For more information regarding the video shown, please contact the speaker.

Imitation: A Core Difficulty

(large effect size)

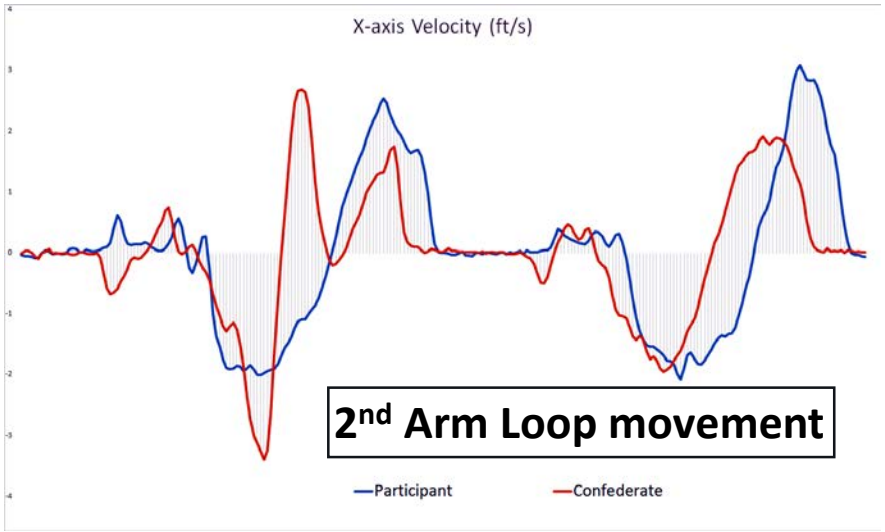
Wearables – gyroscopy, accelerometer

For more information regarding the video shown, please contact the speaker.

Quantifying Imitation Performance

For more information regarding the video shown, please contact the speaker.

Quantifying & Analyzing Movements



Arm loop movement (Confederate – left, Participant – right). To give some insight into the level of tracking fidelity this system is capable of, here is just one of the movements from the Gross motor task. This is on the second circle of movement where the subject has started to adapt to mimicking the movement very well. However, you can see subtle differences in the execution of this movement, in both the spatial location of the execution, as well as in the delay in the changes in velocity along the x-axis. So we are not sacrificing signal by not having cords strapped to the patient's body. In other words, if an abnormality exists in motor ability, there is confidence that we will find it with this technology.

Synchronous Motor Learning: Dance

For more information regarding the video shown, please contact the speaker.

Gross Motor Assessment: “Portable”

For more information regarding the video shown, please contact the speaker.

Diagnosing Autism from a 3 Minute "Get to Know" Conversation

Proof of Concept Pilot Study

17 ASD, 27 TD

Age and IQ matched

For more information regarding the video shown, please contact the speaker.

Example of a Predictive Feature

17 ASD, 27 TD

Age and IQ matched

Analyses:

- Machine Learning
- 44 fold Nested Leave One Out Cross Validation

1st Study Results:

Preliminary/Unpublished

Accuracy: ~84%

For more information regarding the video shown, please contact the speaker.

Limitations: Many. 1st Proof of Concept Study

Computational Linguistics

Two Parts to Speech

- **What we say**: morphemes->sentences (contractions, turn taking)
- **How we say it**: acoustics: rate, tone, rhythm, volume, stress, intensity (prosody, co-articulation: spacing between phonemes/words)

- Quantify both (natural language processing & acoustic analyses)
- Prediction – diagnosis, treatment response, brain scan result, genomic risk factors, etc.

Example pilot study findings (Parish-Morris et al, 2016)

- Use pedantic phrases/odd word choices: 85% AUC (n=65 ASD & 17 TDC)
- More dysfluencies (Um, Uh); Slower speech rate; Longer inter turn pauses, Differences in Pitch (fundamental frequency)
- Best prediction: Multivariate analyses combining speech features with nonverbal communications (facial expressions, eye gaze, gesture) and imitation

Perceptual Computing Promises

Improvements in Clinical Care (not autism specific)

- Reduction in clinic waitlists with remote Screening Assessment & Triage
- Earlier, more accurate diagnosis → earlier intervention → better outcomes
- Ongoing home and school based *monitoring* of response to interventions

Improved Scientific Reproducibility

- Characterize Heterogeneity → Control Heterogeneity
- Scalable to the real world assessment enabling larger samples

Accelerate biological discovery: genetics, brain imaging, etc.

- Impoverished characterization, e.g., "autism" vs. "no autism," handicaps biological studies
  - Statistical modeling imprecise and statistically underpowered

THANK YOU!

Center for Autism Research (CAR)

IACC
INTERAGENCY AUTISM
COORDINATING COMMITTEE

Panel Discussion

IACC
INTERAGENCY AUTISM
COORDINATING COMMITTEE

Break

Meeting of the IACC

Afternoon Agenda - continued

3:40 “Learn the Signs, Act Early” Update

Stuart Shapira, M.D., Ph.D.
Chief Medical Officer and Associate Director for Science
National Center on Birth Defects and Developmental Disabilities Center for Disease Control and Prevention

Learn the Signs. Act Early.

CDC's effort to improve early identification of autism spectrum disorder and other developmental disabilities by empowering parents and other care providers to

'Learn the Signs' of typical development and

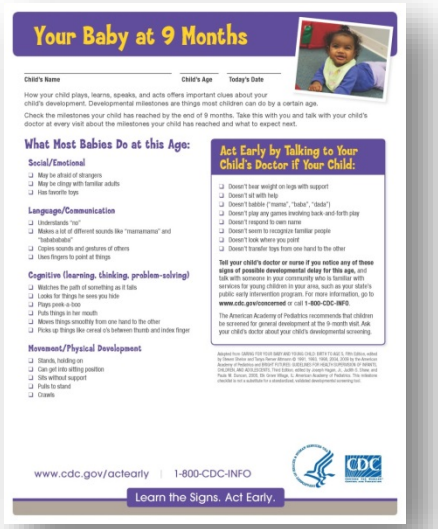
'Act Early' on developmental concerns

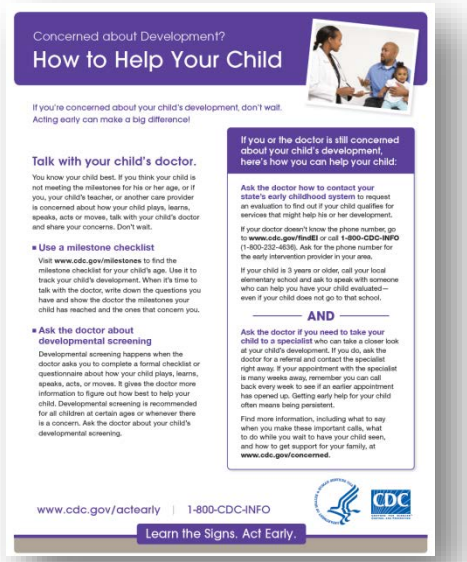
so children and their families can get the services and support they need as early as possible.

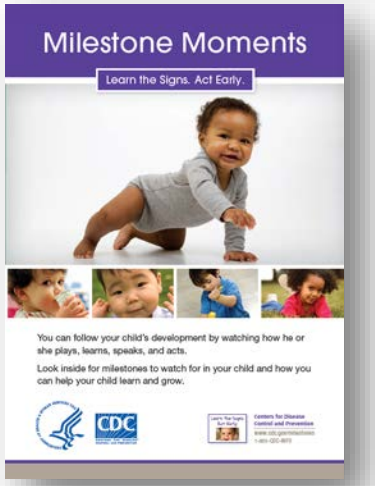
How We Work to Realize Our Mission

- Develop and disseminate high-quality, research-based, parent-friendly materials to engage parents and other care providers in ongoing developmental monitoring through age 5 years
- Provide clear, concrete guidance about what to do when there is a developmental concern

Learn the Signs. Act Early. Materials







Learn the Signs. Act Early. www.cdc.gov/ActEarly

Getting the Materials is Easy

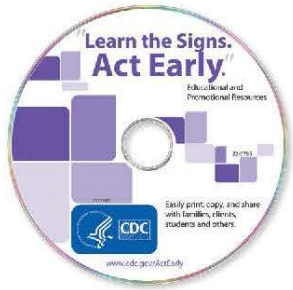
Print FREE materials directly at
www.cdc.gov/ActEarly
(click on "Free Materials")

OR

Print materials from a FREE disk.
Order disk from
www.cdc.gov/ActEarly/Orders

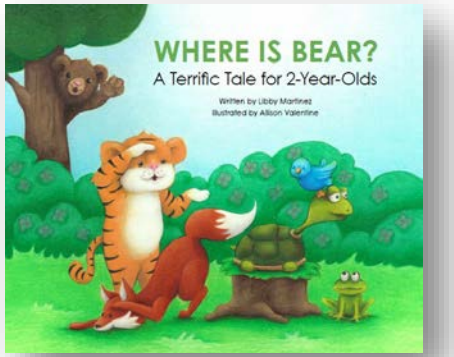
OR

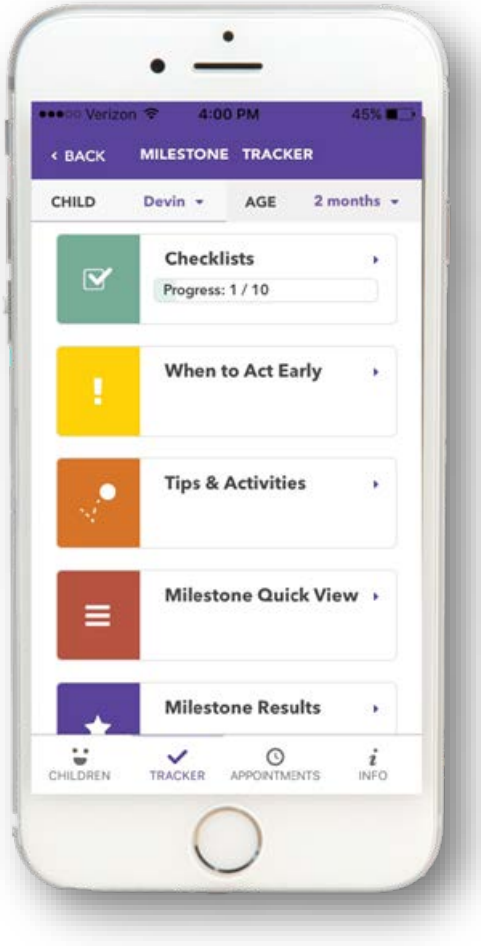
Order FREE printed materials
(in limited quantities) in English or Spanish
from www.cdc.gov/ActEarly/Orders



New Materials and Resources

Where is Bear? A Terrific Tale for 2-Year-Olds (children's book)

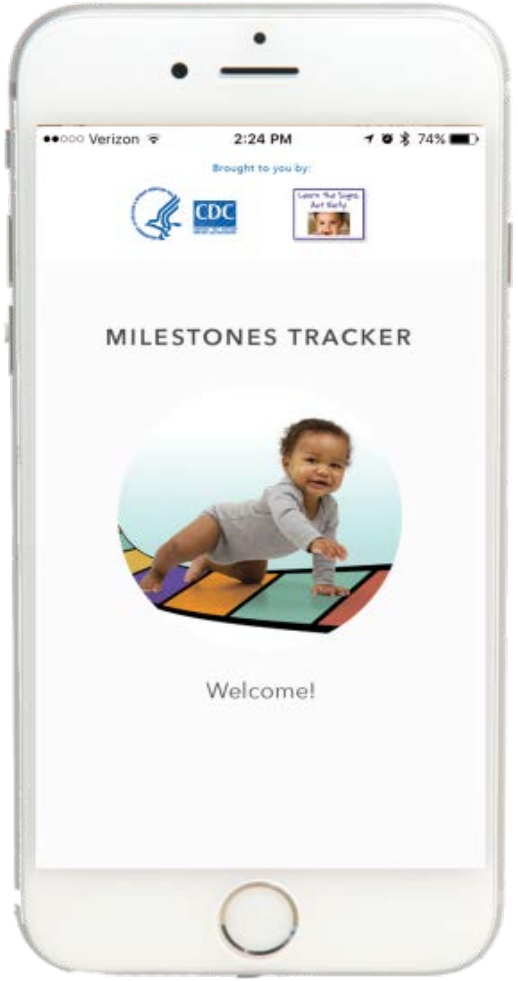




A photo or video for each milestone 2 mo.-5 yrs.!

Milestone Tracker smart phone app
Available this May!

Coming Soon! *Milestone Tracker* App



Milestone Tracker
smart phone app
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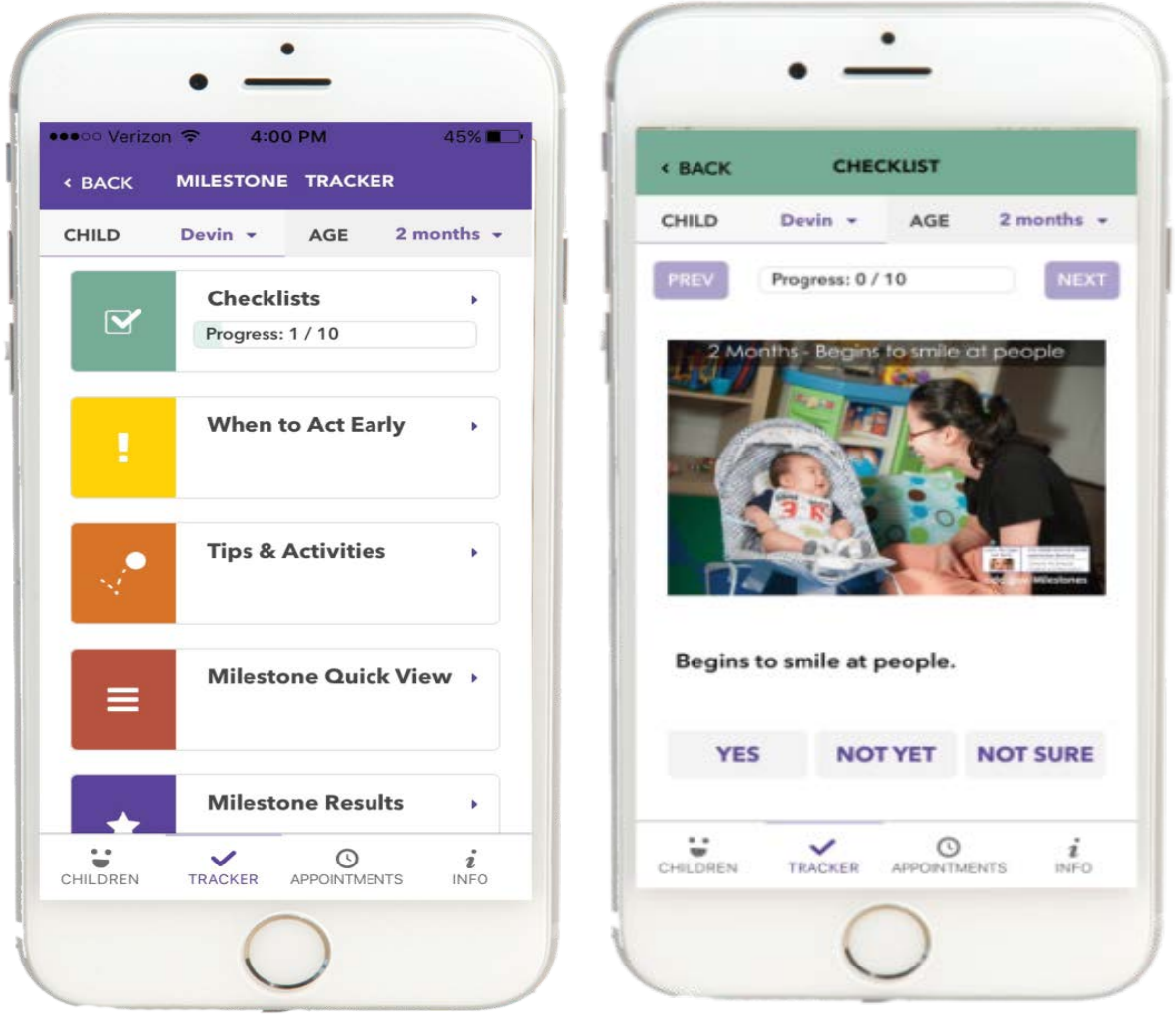
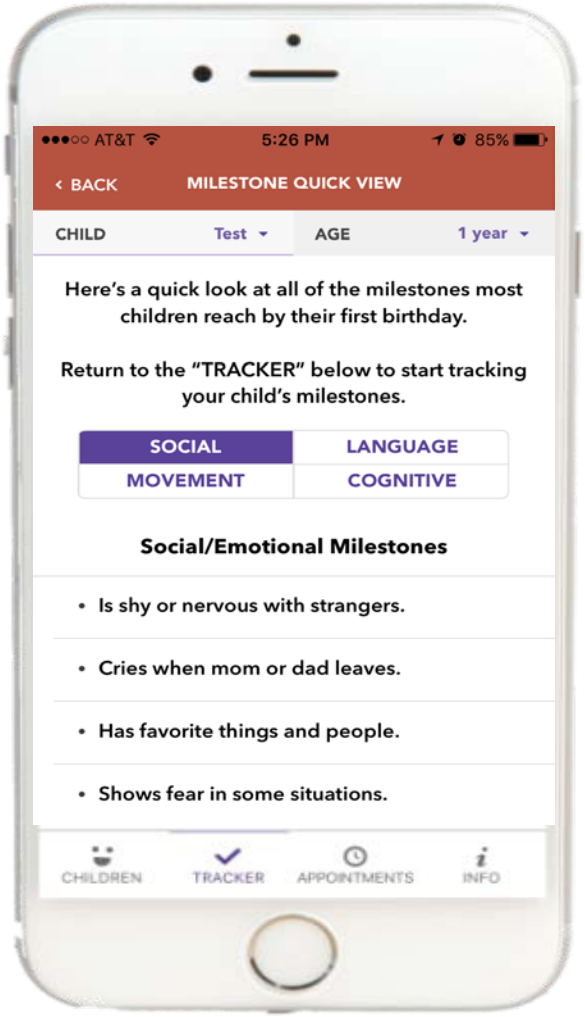
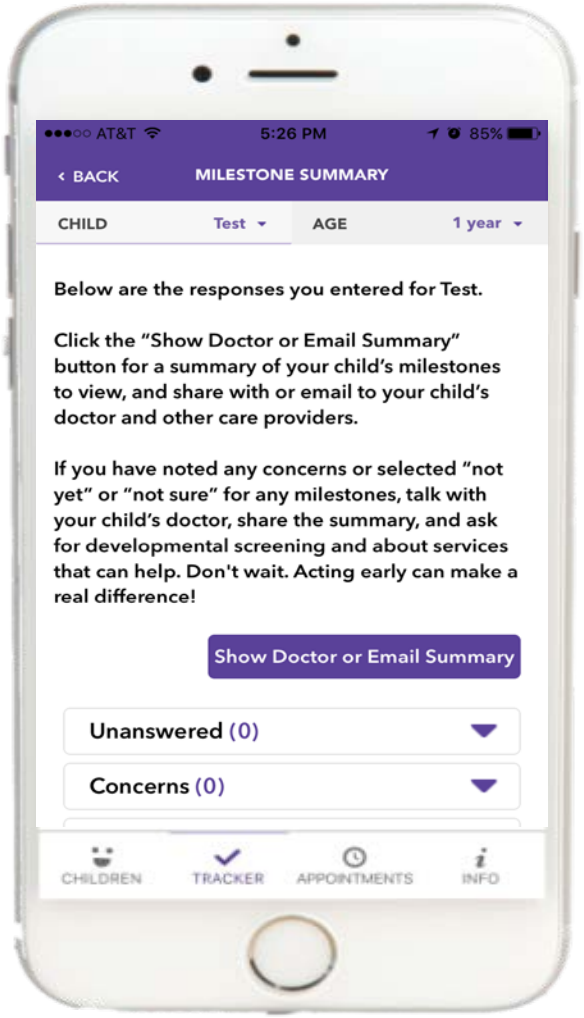
Milestone Tracker App



Learn the Signs. Act Early. www.cdc.gov/ActEarly

Milestone Tracker App





Act Early Ambassadors

- Community champions to increase awareness activities and improve early identification practices
- Serve as state or territory point-of-contact for the national LTSAE program
- **https://www.cdc.gov/ncbddd/actearly/ambassadors-list.html**

Learn the Signs. Act Early. Across Early Childhood Settings and Programs

- ❑ Primary & pediatric health care
- ❑ Care coordination
- ❑ Home visitation
- ❑ Military child care
- ❑ Child welfare
- ❑ Early education & child care
- ❑ Women, Infants, and Children (WIC) nutrition program

For more information, contact
ActEarly@cdc.gov

The findings and conclusions in this presentation have not been formally disseminated by the Centers for Disease Control and Prevention and should not be construed to represent any agency determination or policy.

Meeting of the IACC

Afternoon Agenda - continued

4:00 Summary of Advances Discussion

Susan Daniels, Ph.D.
Director, OARC, NIMH and Executive Secretary, IACC

Karen Mowrer, Ph.D.
Science Policy Analyst, OARC, NIMH

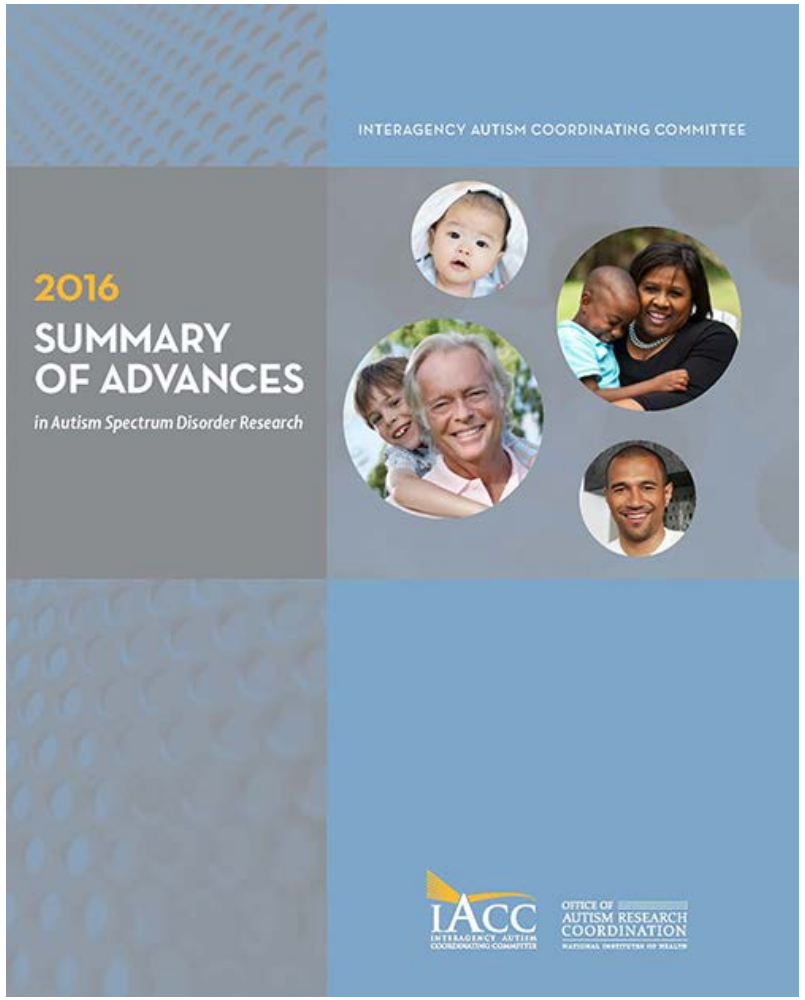
Joshua Gordon, M.D., Ph. D.
Director, NIMH and Chair, IACC

Summary of Advances

Karen Mowrer, Ph.D.
Health Science Policy Analyst
Office of Autism Research Coordination
National Institute of Mental Health

Susan A. Daniels, Ph.D.
Director, Office of Autism Research Coordination
Executive Secretary, IACC
National Institute of Mental Health

Revised Process Was Used to Develop 2016 IACC Summary of Advances



- Annual publication – required by CARES Act
- Lay-friendly summaries of the 20 most significant advances in ASD biomedical and services research, as selected by the IACC
- Covers articles aligning with all seven Strategic Plan Question areas

https://iacc.hhs.gov/publications/summary-of-advances/2016/

Summary of Advances Process

- Was revised to issue requests for nominations throughout the year instead of once a year.
- Required submission of justification with each nomination.
- Nominations discussed at each meeting.
- Some nominations eliminated to narrow the items to be included on the ballot.

OARC used a survey to gather feedback from the IACC about your experience with this process to help with any needed improvements for 2017.

Results of Survey on 2016 Summary of Advances Process

	YES	NO
1. Were you satisfied with the IACC Summary of Advances nomination and voting process in 2016?	10	1
2. Do you feel that there was adequate communication from OARC to IACC members regarding the 2016 IACC Summary of Advances process?	11	0
3. Do you feel that you had an adequate opportunity to nominate articles and express your viewpoints on articles nominated by others for the 2016 Summary of Advances?	11	0
4. Do you feel that the list of nominated articles that appeared on the voting ballot are of sufficient scientific quality and represent appropriately significant advances in the field?	10	1
5. Do you feel that your interests and perspectives are adequately represented in the final 2016 Summary of Advances article selections?	10	1
6. Are you in favor of using the same Summary of Advances nomination and voting process in 2017?	10	1

Summary of Advances Process

- **Monthly solicitation is sent from OARC to collect nominated advances from IACC members**
  - Not many responses received - continue the frequency of the email?
  - Often do not receive justifications - continue justification requirement?
- **Advances are compiled quarterly for discussion at IACC meetings**
  - Conduct vetting more thoroughly during each meeting
- **Final nomination list will be sent out to IACC in January for voting by email ballot**
- **Votes will be counted and tiebreaker will be conducted if necessary**
- **Lay-friendly summaries of top 20 selections will be prepared and circulated to IACC**
- **Publication will be finalized and released in April**

2017 Summary of Advances Nominations

January - April

Joshua Gordon, M.D., Ph.D.
Director, National Institute of Mental Health
Chair, IACC

Meeting of the IACC

Afternoon Agenda - continued

4:30 Round Robin

5:00 Closing Remarks and Adjournment

Meeting of the IACC

Round Robin

Closing Remarks

Meeting of the IACC

Adjournment