Autism Spectrum Disorders: Overview of Clinical Features and Clinical Services

Marcus Autism Center 4th Annual Summer Symposium on Autism Spectrum Disorder

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Emory Center for Translational Social Neuroscience

Thank You

- The children and families who support our clinical and research activities
- The Marcus Foundation
- The J.B. Whitehead and Woodruff Foundations
- The Children's Healthcare of Atlanta Foundation
- The Georgia Research Alliance as well as
- The National Institute of Mental Health
- The National Institute of Child Health and Human Development
- The National Science Foundation
- The Simons Foundation
- The Autism Science Foundation
- Autism Speaks
- United Way

Marcus Autism Center at a glance

- Translation
- Impact
- Clinical Resources
- Research Excellence
- Faculty Advancement
- Research Resources

The Science of Clinical Care

Web of Relationships = Opportunities

Emblematic!

Autism Center of Excellence

Behavioral Neuroscience: infant rhesus monkeys

Social vocal engagement: infants (0 to 36 months)

Social visual engagement: infants (0 to 36 months)

Treatment: infants & toddlers (12 to 14 months)

Web of Relationships

University Partners
- UCP
- UCLA
- Washington University
- Albert Einstein, NY
- Cornell
- Drexel
- Florida State University
- Harvard
- NICHD/Autism Speaks BSRC (> 20 sites)
- Foundation for NIH group

Funding Partners
- NIH
- K23
- F32
- PIREA
- Marcus Foundation
- Woodruff/Whitehead Foundation
- Georgia Research Alliance
- Autism Speaks
- Autism Science Foundation
- Simons Foundation
- United Way

The Science of Clinical Care
Challenges and Opportunities: Reducing Age of Diagnosis & Improving Access to Care

• Brain disorder of genetic origins
• Adverse outcomes can be attenuated
• Importance of early diagnosis and intervention for lifelong outcome and cost of care
• American Academy of Pediatrics—Screening (18 and 24 months), but still low uptake
• 8% of primary care providers routinely screen for ASD
• Median age of diagnosis in US: 4.6 to 5.7 years
• Later still in disadvantaged communities
• No Community-viable system of care
• Reimbursement systems NOT in place

Johnson & Myers, 2007; Dacovic et al., 2006; Heidgerken et al., 2005; Honigfeld et al., 2012; Shattuck et al., 2009; Mandell et al., 2005, 2009

Autism Disrupts the Platform for Brain Development

<table>
<thead>
<tr>
<th>MSH School of Text</th>
<th>Reciprocal Social Interaction</th>
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<tbody>
<tr>
<td>WHITE MATTER DEVELOPMENT</td>
<td></td>
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<td>Protein (months)</td>
<td>Infant (4 weeks)</td>
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<td>Born to Socially Orient</td>
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<td>Neuroplasticity</td>
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H-J Park PhD


Research Enterprise at a glance

Strategy for Research Enterprise

Diagnosis

Behavioral Neuroscience

Animal Models

Genetics

Neurobiology

Psychopharmacology

10 RESEARCH CORES

5 INTERNAL 4 COLLABORATIVE

RESEARCH ADMINISTRATION

INFORMATICS

DATA MANAGEMENT & ANALYSIS

CAUSES

TREATMENT

COMMUNITY-VARIABLE SOLUTIONS

VALUE PROPOSITION

Research Enterprise at a glance

LETTER

Attention to eyes is present but in decline in 2–6-month-old infants later diagnosed with autism

Marente Jones & H-J Park

Deciles in eye contact have been a hallmark of autism (Marente Jones & Park, 2010), and the condition is associated with deficits in the development of the visual system. We report a study of 80 infants, aged 2–6 months, who were later diagnosed with autism spectrum disorders using a standardized naturalistic eye-contact task. We found that the infants who later developed autism showed a decrease in eye contact from 2 months to 6 months of age. This finding suggests that eye contact may be a useful predictor of autism spectrum disorders in infancy. However, the association between eye contact and autism spectrum disorders is complex and may be influenced by various factors, such as maternal behavior and infant temperament. Further research is needed to better understand the role of eye contact in the development of autism spectrum disorders.
Translational Opportunities

• High-throughput, low-cost, deployment of universal screening in the community
• Early detection, early intervention, optimal outcome
• Prevention or attenuation of intellectual disability in ASD

Molecular Genetics at Emory

Steve Warren
Mike Zwick
Jan Muhe
Peng Jin
David Cutler

Michael Gambello

ACE Network

Under-represented populations

The next 10 years of genetics research

Guidelines for investigating causality of sequence variants in human disease

Ontogeny & Neural Basis of Social Visual Engagement in Monkeys

Yerkes Field Station, Lawrenceville GA
> Never separated from mom
> Remain in social group

Jocelyne Bachevalier, PhD

Xiao Ping Hu, PhD

Lisa Parr, PhD

Ontogeny & Neural Basis of Social Visual Engagement in Monkeys

In vivo diffusion MRI data showing major white matter pathways in a 2-week-old rhesus macaque.

Jocelyne Bachevalier, PhD

Longchuan Li, PhD
Community-Viable Solutions:

- United Way new $1.875 m/3 yrs (Jennifer Stapel-Wax PI)
- NIH Multi-Site R01: Marcus, Cornell, Drexel, FSU (May 2014)
- Already work in Atlanta, several GA counties, as well as in Fl, PA, TN and NY

“Less than 20% of children with Autism in the US are identified before the age of 3 years”

Augmenting Access to Early Treatment via Partnerships

Family  
Primary Care Physician  
Early Intervention Provider

COLLECTION OF TOOLS
- About Autism
- Early Intervention Providers
- Primary Care Physicians
- Family Engagement

Brief & Selective Overview of Autism Spectrum Disorders

Autism is ... in 1943 as in 2014
**Evolutionarily Highly Conserved and Developmentally Early Emerging Mechanisms of Socialization**

Normative social development: Infants come into the world “pre-wired” for social engagement

- From the first days of life infants are profoundly sociable
- Human face and human voice are the most interesting stimuli in the environment
- Early emergence of
  - selective attention
  - selective engagement
  - social reciprocity
  - attachments
  - social-communication skills
  - joint attention and social referencing skills
  - “Theory of Mind”
  - relationships

**Autism:**

Unlike in typical development, predispositions to orient to, and engage with people are absent or impaired.

**Developmental Trajectories**

- Developing expertise about the Social World
- Developing expertise about the Physical World
Core Challenges aka Realities

- **SOCIAL SKILLS**: the intangibles, the unstructured, the novel, the implicit, the intuitive, the “common sense”, the mentalistic
- **COMMUNICATION SKILLS**: the informal, the conversational, the reciprocal, the ‘other-directed’, the polite, the ‘untrue’, the ‘chatty’
- **ADAPTIVE SKILLS**: grooming and self-care, domestic chores, ‘survival skills’, living in the community, functioning in bureaucracies, groups and relationships, legal concerns
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Self-help: a non-exhaustive list

- Personal hygiene
- Grooming
- Minor or annoying health issues
- Major health issues
- Clothing: purchasing, care, choice, when and how
- Mores and regulations
- The private vs. the public
- Puberty related
- Sexuality
- ...

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Domestic: a non-exhaustive list

- Purchasing needs: the when, where, and how
- Eating and cooking: purchasing, planning, preparation, eating out (e.g., cafeterias), eating out (e.g., at friends’)
- Fixing and mending
- Knowing when doing oneself, when seeking help
- Knowing when one needs to fix anything
- Cleaning and organizing
- What to throw out and what to keep
- Hoarding
- Paying bills, budgeting, money matters (e.g., banking)
- Negotiating privacy
- Rigidities, rituals, obsessionality
- ...

Community and survival skills: a non-exhaustive list

- Going to places, transportation
- Emergencies
- Dealing with social annoyances (e.g., panhandlers, manipulators, exploitative companions)
- Dealing with people in position of authority
- POLICE
- Rules, the law, the novel, the unexpected
- The private, the public, the acceptable, the seemingly criminal, the self-incriminating, the poor self-advocate
- The bureaucracies, the forms, the scheduled commitments
- The telemarketers, the soliciting, the “too good to be true’ invitations and offers, ‘junk’ mail, INTERNET
- ...

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Social Attribution Task: narrative samples
Typically Developing Adolescent boy, age 13-9, FSIQ = 112

“... What happened was that the larger triangle -- which was like a bigger kid or a bully, and he had isolated himself from everything else until two new kids come along and the little one was a bit more shy, scared, and the smaller triangle more like stood up for himself and protected the little one. The big triangle got jealous of them, came out, and started to pick on the smaller triangle. The little triangle got upset and said like “what’s up”? “why are doing this?’ …

Social Attribution Task: narrative samples
Adolescent boy with autism, age 14-9, FSIQ = 115

“The big triangle went into the rectangle. There were a small triangle and a circle. The big triangle went out. The shapes bounce off each other. The small circle went inside the rectangle. The big triangle was in the box with the circle. The small triangle and the circle went around each other a few times. They were kind of oscillating around each other, maybe because of a magnetic field. After that they go off the screen. The big triangle turned like a star - like a Star of David - and broke the rectangle ...”

Thinking about things and thinking about people

Searching for Social Meaning in Real-life Situations

38 year old adult with autism (normative IQ)

- Starts when a small equilateral triangle breaks out of a square. A small sphere or circle appears and slides down the broken rectangle. The triangles were either equilateral or isosceles. Later the small, I think, isosceles triangle and sphere bounce around each other, maybe because of a magnetic field ...

- The rocket is being launched and is in preliminary orbit around the earth, winding around the moon at the appropriate distance so that the satellite can be released. The satellite was launched from the rocket, and it actually landed on the moon. The satellite was actually more like a lunar module ...
Following Social Attention Cues


Tracing the Shape of a Social Triangle

Viewer with Autism
Typically Developing Viewer

Following Social Attention Cues


Following Social Attention Cues

Typically Developing Viewer

Following Social Attention Cues

Viewer with Autism
Focus on the Non-Speaker: contextual cues that may alter the meaning of a social scene

Three main principles of social and communication skills learning

- Awareness of conventional rules of social engagement and social conversation
- Active and appropriate ‘reading’ of social cues
- Self-monitoring and adjustment in conversation

Active ‘reading’ of social cues

- Important for adjusting, predicting, ‘regrouping’
- Eye contact / gaze
- Facial and bodily gestures / posture
- Prosodic cues (volume, inflection, rate)
- ‘Integrative’ cues
- Practice in concrete situations (rehearsals, role-taking)
- Different settings – going from small therapeutic to larger naturalistic (back and forth)

Awareness of conventional rules

- Topic selection
- Ways of marking topics shifts
- Background information (presupposition and familiarity)
- Knowledge base of potential conversational partners
- Repertoire of interests that can be discussed
- Conversational expectations (turn-taking, listening, building on what is said)
- Pertinence, ‘quantity’, … (rules of pragmatics)

Self-monitoring in conversation: Adjustments

- Style/register (e.g., more or less formal)
- Volume (e.g., in terms of social setting, proximity, number of people, and background noise)
- Inflection modulation
- Rate, rhythm, and stress (e.g., emphasis, affective communication)
- Awareness of self style
- The utilization of feedback (provided by others)
What does it take to understand a social situation?
Or HOW TO BUILD A SOCIAL SKILLS TRAINING CURRICULUM

Salience

Salience

Salience

Pertinence

Theory of Mind: Cognition

Prettiest girl
I have ever seen!
What does it take to understand a social situation? OR HOW TO BUILD A SOCIAL SKILLS TRAINING CURRICULUM

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Theory of Mind: Cognition

What a SHOW-OFF!!

Theory of Mind: Affect

Mad. Jealous.

Theory of Mind: Affect

Self-Love.

Inferring Social Context:

It is a costume contest. The two girls are mad because the other one attracted all of the attention.
Autism Spectrum Males (n = 20)

Normal Controls Males (n = 20)

Absence of Fusiform Activation To Faces

t maps of mean % signal change, p < .01
Masked for face-baseline & object-baseline at .05

The neuroanatomy of face recognition: the Fusiform gyrus

Underside of actual brain

Coronal MRI slide along the dotted line

Same or different person?

Same or different object?
Differences in Object “Saliency” – falling in love with Digimon

“Digimon” (Digital Monsters)

Greater Interest/Attention to Digimon than People

- Fusiform activation for Digimon characters
- Amygdala activation for Digimon characters
- Atypical specialization of ‘FFA’
- Emotional involvement and investment in circumscribed interests

Grelotti et al., 2005, Neuropsychologia

Exceptional drawing ability

Typical 8 yr old

Nadia: around 4 or 5

Exceptional drawing ability

Typical 8 yr old

Nadia: around 4 or 5

Exceptional drawing ability

Stephen Wiltshire MBE http://www.stephenwiltshire.co.uk/

However
Learning about autism from exceptional abilities

Illustration 1: Natural grasp of perspective ('Underground station')

Illustration 2: Partial excavation

Illustration 3: Technical drawing
Learning Style

- Learning ABOUT the world, not necessarily learning how to function in the world
- Parts to wholes – unfortunately, the world is wholes to parts
- Rote and associative; unfortunately learning needs to be integrative and conceptual
Circumscribed interests

- Frequent and highly visible manifestation of the condition
- Monopolizes learning
- Monopolizes thinking
- Monopolizes conversation and relationships

Some examples

- on snakes
- Writings of incarcerated people
- On death and dying
- Religion
- Cul-de-sacs
- Deep-fat-fryers
- Shakespeare’s plays
- Telephone pole insulators
- Pokemon
- Digimon
- Weather
- TV/radio stations
- Electrical fans
- Photographing people
- Computer serial numbers
- Large numbers
- Algebraic equations

Potential for catastrophic consequences

- DANGER!! Interests and repetitive behaviors get caught together (e.g., touching, shoes, fetish)
- DANGER!! Internet, solitary and unmonitored use of computer, pornography on the web
- The dangerous combination of computer technical skills and naivety + lack of street smarts may lead to problems with the law
- Not potential victimizers, but the law often does not make that distinction (mandatory sentences)

Importance for Self-Identity and Self-Esteem

- Circumscribed interest may be important pillar of self-identity
- Very important to take this very seriously
- Examples:
  - Cui de sacs
  - Gaining insight into people through mathematics (e.g., algebraic equations)
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Executive Dysfunction

- Being devoid of a ‘pilot’ or ‘navigator’
- The CEO has taken a long-term vacation
- Mothers and frontal lobes
- Requiring help with trivial matters such as shopping and completing assignments
- Organizing their own activities in a goal-directed fashion
- Completing tasks in an efficient manner
- Learning from ongoing experiences
- Breaking down tasks into stepwise algorithms
- To do lists, organizers, new technology

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Obstacles to Successful Adaptation

- Anxiety, panic, fears, phobias, depression and despondency, motivational issues, rigidities, ...
- Behavioral approaches (functional behavioral assessment)
- Psychopharmacological approaches
- Need for synergy: social-communication, real-life situations, comprehensiveness
- Need for integration: generalization across people and across settings
- Building on strengths – Avenues for success
- Managing difficult behaviors: ‘fits’, ‘rumination’, ...

Vocational Training

- Emphasis on addressing social disabilities, eccentricities, and anxiety-related vulnerabilities
- Grooming, presentation, application letter writing, as well as every aspect of the job interview process
- Neuropsychologically informed
- College/vocational experience is facilitated by individual supervision/tutorial system
- Socially less demanding
- Acquaintance with supported college or work resources (e.g., job coaches, transition agencies, parent support networks)

Because Celine asked me to talk about DSM-5

From Early Childhood Autism, to Pervasive Developmental Disorders, to Autism Spectrum Disorders: Kanner & DSM ology

- Pervasive Developmental Disorders (early onset disorders of socialization)
  - With or without intellectual disabilities
    - Autistic disorder, PDD-NOS
  - Without intellectual disabilities
    - Asperger’s disorder
  - Always intellectual disabilities
    - Rett’s disorder
    - Childhood Disintegrative Disorder

DSM-5 workgroup reasoning

- “ASD” for Autism, Asperger Syndrome, CDD, PDD-NOS
  - ASD vs ‘neurotypically’ or non-ASD conditions valid
  - Subtyping not reliable; better mediators: severity, language level or intelligence
  - Best ASD + associated features

- 3 domains become 2
  - Social/Communication are inseparable
  - Language delays not specific to ASD: mediator
  - Better psychometric properties (better specificity: same sensitivity)
  - Examples across ages and levels of severity

- Smaller number of symptoms
  - Multiple criteria in DSM-IV, same symptom
  - Data analyses (research on criteria) - SSC large sample

- DSM-5 vs. DSM-IV-TR
  - 56 Studies published so far focused on DSM-5 (by 2013)
  - ~ 10 studies comparing Se & Sp of DSM-5 relative to DSM-IV

DSM-5 definition of ASD

Social-Communication

- Persistent deficits in social communication and social interaction across multiple contexts, currently or by history: (all 3)
  - Deficits in social emotional reciprocity (from abnormal social approach and failure of back-and-forth conversation; to reduced sharing of interests, emotions, etc.)
  - Deficits in nonverbal communicative behaviors used for social interaction (from poorly integrated verbal and nonverbal communication, to abnormal eye contact, etc.)
  - Deficits in developing, maintaining, and understanding relationships (from difficulties adjusting behavior to suit various social contexts to in making friends, absence of interest in peers, etc.)

Restricted, Repetitive Behaviors

- Restricted, repetitive patterns of behavior, interests or activities, current or by history: (2 of 4)
  - Stereotyped or repetitive motor movements, use of objects, or speech;
  - Insistence on sameness, inflexible adherence to routines, or ritualized patterns of verbal or nonverbal behavior;
  - Highly restricted, fixated interests that are abnormal in intensity or focus;
  - Hyper- or hyporeactivity to sensory input or unusual interest in sensory aspects of the environment;
DSM-5 definition of ASD

- Symptoms must be present in the early developmental period (may not be fully manifest until social demands exceed limited capacities, or may be masked by learned strategies in later life).
- Symptoms cause clinical significant impairment in social, occupational, or other important area of current functioning;
- Not better explained by intellectual developmental disorder or global developmental delay (discrepancy between social communication skills and intellectual ability);
- If child/individual met DSM-IV criteria for autistic disorder, Asperger’s, or PDD-NOS (well-established), DSM-5 diagnosis of ASD applies;
- If marked deficits in social communication, but does not meet criteria for ASD, evaluate for Social (Pragmatic) Communication Disorder (i.e., no symptoms in the 2nd domain).

Specify:
- if intellectual impairment
- if language impairment
- if associated with known medical or genetic condition or environmental factor (additional code)
- if associated with another neurodevelopmental, mental, or behavior disorder
- if catatonia (????!!)

No more multi-axial system (of DSM-IV)

Severity Levels of ASD
- Separate for Social Communication, and for Restricted, Repetitive Behaviors
- Level 3: Requiring very substantial support
- Level 2: Requiring substantial support
- Level 3: Requiring support

DSM-5 definition of Social (Pragmatic) Communication Disorder

- Persistent difficulties in the social use of verbal and nonverbal communication:
  - Deficits in using communication for social purposes, such as greeting and sharing information appropriate to social context
  - Impairment of the ability to change communication to match context or the needs of the listener (such as speaking differently in, and adjusting to different contexts)
  - Difficulties following rules for conversation and storytelling (taking turns in conversation, rephrasing when misunderstood, using verbal and nonverbal signals to regulate interaction)
  - Difficulties understanding what is not explicitly stated (making inferences) and nonliteral or ambiguous meanings of language (metaphors, humor, irony)
- Deficits result in functional limitations in effective communication, social relationships, academic achievement, or occupational performance

Onset: early developmental period (but deficits may not become fully manifest until social communication demands exceed limited capacities)

Symptoms not attributable to another medical or neurological condition, low abilities in word structure and grammar

Symptoms not better explained by ASD, intellectual disability, global developmental delay or another mental disorder.

"Rare < 4 years"; Variable outcome

Risks: family history of ASD, communication disorders, specific learning disorder.

Is this a back door to “Broader Autism Phenotype” (BAP) moved outside its original (ASD) familial context?

ASD without RRBs (current or by history!)

Other rule outs: ADHD, Social Phobia, ID

Advocacy Groups’ position and concerns

- Misdiagnosis or underdiagnosis of people with Asperger’s Disorder
- “Asperger’s” has meaning to individuals affected, families, service providers, organizations, communities, the general public
- Symptoms not comprehensive enough:
  - sensory atypicalities, anxieties, Executive Dysfunction, RH learning difficulties - important for treatment/educational programming
- Scales for measurement of ASD diagnostic criteria not released yet -> Indices of Severity

Less Discussed Complexities

- The dependency upon ADI-R and ADOS
  - who administers these instruments
  - reliability at the item level
  - Doing away with the experienced clinician
- Where are the challenges most felt
  - Are these challenges captured by the instruments
  - The need for real-life instrumentation
- The “subthreshold” symptoms
  - A “milder” social disability
  - The real-life consequences of defining it as “mild”
- Self-representation
- The reality of community-based practices: the importance of DSM
QUO VADIS
“diagnostic process” and DSM-5

- All encompassing definition: need for quantification and individualization
- Need for “tests” that are both diagnostic and prescriptive
- Redefining autism/ASD for the biological sciences (NIMH)
- What is “core” and what are “associated disabilities”
- Could these associated disabilities be significantly attenuated if not prevented?

Now you truly deserve to go to lunch ...
Have a wonderful symposium!
It will be terrific!

Thank you