Overview

• Autism in infants and toddlers
  – What we knew from home movies + screening studies
• Developmental models of autism
  – Informed by understanding of typical development
• The new science of autism in infancy
  – Studying at risk siblings
• Relevance for early intervention
Earliest signs identified in home movies

- **Advantages**
  - ‘Blinded’ (as diagnosis is not yet known)
  - Naturalistic

- **Limitations**
  - Data not standardized
  - Parents may not film toddlers when showing behaviours most of interest (e.g. ‘odd behaviours’)
  - Do not know how specific the signs are to autism

Dawson et al. (2004) *Development & Psychopathology*
Earliest signs identified in home movies

<table>
<thead>
<tr>
<th>Time period</th>
<th>Behaviour</th>
<th>Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Less attention to social stimuli</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Reduced affect</td>
<td></td>
</tr>
<tr>
<td>~12 months +</td>
<td>Reduced response to name</td>
<td>Adrien et al (1991, 1993)</td>
</tr>
<tr>
<td></td>
<td>Less joint attention</td>
<td>Osterling &amp; Dawson (1994); Werner &amp; Dawson (2005)</td>
</tr>
<tr>
<td></td>
<td>Abnormal eye contact</td>
<td>Baranek (1999)</td>
</tr>
<tr>
<td></td>
<td>Reduced looking at people</td>
<td>Ozonoff et al (2008) + others</td>
</tr>
<tr>
<td></td>
<td>Motor abnormalities</td>
<td></td>
</tr>
</tbody>
</table>
Earliest signs that predict diagnosis (in population screening studies)

- Lack of joint attention behaviours
  - Gaze monitoring, pointing for interest
- Reduced response to name
- Lack of early pretend play
- Reduced range of early play behaviours
- Impoverished range of facial expressiveness
- Reduced interest in people

The new science of autism in infancy

**REVIEW ARTICLE**

What are Infant Siblings Teaching Us About Autism in Infancy?

Sally J. Rogers

**EDITORIAL**

Getting answers from babies about autism

Mayada Elsabbagh and Mark H. Johnson
Allows us to study autism as it emerges

• 5% to 10% of younger siblings will go on to have ASD
  – May be higher in self-selecting research samples
• One goal is to identify the earliest signs of the disorder
  – Behavioural signs
  – Neural responses in addition to behaviour
• Allows as to study the ‘broader autism phenotype’
  – Some features might characterise the ‘at risk’ group but not predict autism outcomes
  – This ‘recovery’ pattern might inform genetic and environmental influences on brain development

Getting answers from babies about autism

Figure 4. Hypothetical trajectories for expression of risk in infant siblings at both neural and behavioural levels. The ASD trajectory is characterised by a high-dose of mediating risk factors, the impact of which becomes compounded and amplified over time. The BAP characterises infants with a low-dose of risk factors leading to sub-clinical expression of the condition. Canalisation involves similar initial expression of risk but eventual restoration of the typical developmental trajectory.
The prodrome of autism: early behavioral and biological signs, regression, peri- and post-natal development and genetics

Noa Yirmiya1 and Tony Charman2
1Department of Psychology and School of Education, The Hebrew University of Jerusalem, Israel; 2Centre for Research on Autism and Education, Institute of Education, London, UK

Table 1. Characteristics of ASD emerging between 12 and 24 months. Early signs are variable and initially have low predictive value that then increases with age

<table>
<thead>
<tr>
<th>Deficits and delays in emerging joint attention [17,18]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased response to name [19]</td>
</tr>
<tr>
<td>Decreased imitation [15]</td>
</tr>
<tr>
<td>Delays in verbal and non-verbal communication [20]</td>
</tr>
<tr>
<td>Motor delay [17]</td>
</tr>
<tr>
<td>Elevated frequency of repetitive behaviours, e.g. hand waving [21]</td>
</tr>
<tr>
<td>Atypical visuo-motor exploration of objects [22]</td>
</tr>
<tr>
<td>Extremes of temperament [23]</td>
</tr>
<tr>
<td>Decreased flexibility in disengaging visual attention [15]</td>
</tr>
</tbody>
</table>

Grand Averaged Waveforms

N290

P400

Latency (msec)

Low-Risk (N = 20)

High-Risk (N = 20)

Faces

Objects

Latency (msec)

Low-Risk (N = 20)

High-Risk (N = 20)

Faces

Objects
Gaze behavior and affect at 6 months: predicting clinical outcomes and language development in typically developing infants and infants at risk for autism

Gregory S. Young,1 Noah Merlin,2 Sally J. Rogers3 and Sally Ozonoff4

Table 3  Clinical outcomes by risk group and eye-mouth index cluster

<table>
<thead>
<tr>
<th>Risk group</th>
<th>No Concerns</th>
<th>Other Concerns</th>
<th>Speech-Lang. Delay</th>
<th>Autism/ASD</th>
</tr>
</thead>
<tbody>
<tr>
<td>High risk</td>
<td>15</td>
<td>4</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Low risk</td>
<td>19</td>
<td>3</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Eye-mouth cluster</td>
<td>19</td>
<td>3</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>LLL</td>
<td>6</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*Other = global developmental delay; anxiety, oppositional behavior.

HIII = high eye-mouth index scores throughout all still-face conditions (i.e., preferential looking toward the eyes); LLL = low eye-mouth index scores only during unresponsive still-face condition; LLI = low eye-mouth index scores (i.e., preferential looking toward the mouth).
BASIS (British Autism Study of Infant Siblings)

- Led by Mark Johnson and Mayada Elsabbagh (CBCD BABYLAB, Birkbeck College, London)
- Collaborators
  - Tony Charman (IOE), Patrick Bolton (IOP), Simon Baron-Cohen (Cambridge), Jonathan Green (Manchester), Declan Murphy (IOP)
- Funding
  - MRC, Autistica, Autism Speaks (USA)
- [www.basisnetwork.org.uk](http://www.basisnetwork.org.uk)
BASIS Phase 1 (50 high-risk + controls)

<table>
<thead>
<tr>
<th>6-9 m</th>
<th>12-15 m</th>
<th>24 m</th>
<th>36 m</th>
</tr>
</thead>
<tbody>
<tr>
<td>Face scanning</td>
<td>Face scanning</td>
<td>Face pop-out</td>
<td>Face pop-out</td>
</tr>
<tr>
<td>Face pop-out</td>
<td>Face pop-out</td>
<td>Referential learning</td>
<td>Referential word learning</td>
</tr>
<tr>
<td>Gaze following</td>
<td>Gaze following</td>
<td>Fast-mapping</td>
<td>False belief (action anticipation)</td>
</tr>
<tr>
<td>Gaze direction discrimination (EEG)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>The “gap” task</td>
<td>The “gap” task</td>
<td>The “gap” task</td>
<td>The “gap” task</td>
</tr>
<tr>
<td>Anti-saccades</td>
<td>Spatial conflict</td>
<td>Spatial conflict</td>
<td></td>
</tr>
<tr>
<td>Attention</td>
<td>Communication</td>
<td>Interest in people</td>
<td></td>
</tr>
</tbody>
</table>

Network Protocol

<table>
<thead>
<tr>
<th>Measure</th>
<th>Visit 1 (6-9 m)</th>
<th>Visit 2 (12-15 m)</th>
<th>Visit 3 (24 m)</th>
<th>Visit 4 (36 m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parent report</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vineland Adaptive Behavior Questionnaire</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>MacArthur Communication Development Inventory (CDI)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Infant Behavioural Questionnaire (IBQ) / Early Childhood Behavior Questionnaire (ECBQ)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Toddler Early Development Inventory Q-CHAT</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Social Responsiveness Scale (SRS)</td>
<td></td>
<td></td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Feedback from parents on project</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Lab (or home visit)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Demographics</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Medical history</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Mullen Scales of Early Learning</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Head circumference</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Autism Observation Scale for Infants (AOSI)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Autism Diagnostic Observation Schedule (ADOS)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Autism Diagnostic Interview (ADI)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Parent Child Interaction (PCI)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Psychosocial Development and Wellbeing Assessment (DAWBA)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Social Communication Questionnaire (SCQ)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>
Gap task – Testing ‘sticky attention’

Visual orienting in the early broader autism phenotype: disengagement and facilitation

Mayada Elsabbagh, Agnes Volein, Karla Holmboe, Leslie Tucker, Gergely Cibra, Simon Baron-Cohen, Patrick Bolton, Tony Charman, Gillian Baird, and Mark H. Johnson


Neural Correlates of Eye Gaze Processing in the Infant Broader Autism Phenotype


Biological Psychiatry 2009;65:31–36
© 2009 Society of Biological Psychiatry
Gaze Following Task: Eye-tracking.

- Experimental measure of gaze following.
- High ecological validity.
- Precursor to joint attention.

Two measures of gaze following: **first look** & **looking time** to the congruent object on correct first look trials.

Modeling interactions in the developing brain

- Autism emerges over the first three years from subtle and variable differences emerging in the first year
- Infants at-risk who do not go on to a diagnosis share some of the early brain functioning but do not go on to a diagnosis
- Variable pathways reflect multiple gene x environment interactions unfolding over time

_Elsabbagh & Johnson, TICS 2010; Elsabbagh et al. Prog Brain Res, 2011_
Response to eye gaze in infants at-risk

Elsabbagh et al., 2009, Bio Psych

Inhibitory control in infants at-risk: The Freeze-Frame task

Holmboe et al. Infant Beh & Dev 2010
Social and attention predictors of autism related characteristics

Response to eye gaze (n=16)  Inhibitory control (n=22)

<table>
<thead>
<tr>
<th>10-months</th>
<th>36-months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct</td>
<td>Social</td>
</tr>
<tr>
<td>Averted</td>
<td>Communication</td>
</tr>
<tr>
<td>P1 N290 P400</td>
<td>(range: 0-14)</td>
</tr>
<tr>
<td>Boring looks</td>
<td>(range: 0-10)</td>
</tr>
<tr>
<td>Interesting looks</td>
<td>(range: 0-6)</td>
</tr>
</tbody>
</table>

Elsabbagh et al. Prog Brain Res 2011

Infants at risk for autism as a model for studying developmental interactions

- Variability in development of infants at risk is likely to be the result of dynamic and probabilistic interactions over development
- Autism-related characteristics in infant siblings who do not have a diagnosis map dimensionally onto brain function predictors in infancy across multiples social and non-social domains
- Systematic study of these variations can offer important clues toward understanding the emergent nature of autism
BASIS Phase 2

• 75 high-risk sibs + controls
• Babies seen at 4m, 8m, 14m, 24m and 36m of age 14 experimental tasks, including eye-tracking, ERP, EEG and behavioural tasks
• Subgroup: Structural + functional imaging + NIRS at 4 months
• Including a pilot, ‘proof of concept’ RCT of parent early intervention at 8 months of age
  – i-BASIS

i-BASIS team

*University of Manchester*
Jonathan Green, Ming Wai Wan, Samina Holsgrove, Janet McNally, Clare Holt, Janine Lamb

*Birkbeck College, London*
Mark Johnson, Mayada Elsabbagh, Lesley Tucker, Helen Ribeiro, Jeanne Guiraud, Janice Fernandes

*Institute of Education, London*
Tony Charman

*Guys Hospital, London*
Vicky Slonims, Rhonda Booth

*Institute of Psychiatry, London*
Andrew Pickles, Patrick Bolton
Technique

- Core intervention based on Video Interaction to Promote Positive Parenting (VIPP, Juffer et al 2004)
- Additional techniques to adapt to early atypicalities
- Parent-mediated video-aided, home based
- Manualised
- 12 sessions over 5 months
- Procedures to
  - Enhance sensitivity of response
  - Increase shared enjoyment, joint attention, communicative synchrony
  - Specifically address details of early atypicality
  - Aid generalisation (written material, feedback, videos)

Procedure

- Video of free play/naturalistic meal time/face to face interaction – watch and discuss with parent
- Sequential themes
  - Infant watching
  - Speaking for the baby – inferring intentionality
  - Sensitivity chains – synchronous responding
  - Generalising to mealtime and other activities
  - Sharing feelings – affect matching
  - Sharing talk – promoting communication
- Adapting to ‘atypicality’
  - Inflexible attentional style, Face preference and visual face processing, Affect Matching and Reciprocity, Reactivity, Atypical Sensory Behaviours, Social Babble/early communication
RCT design

**Design**
- 2 site 2 arm parallel group RCT of intervention/no intervention; N=50 (following a pilot case series N=8)

**Sampling**
- Infant siblings in BASIS - not selected for atypicality

**Assessment**
- ‘Vertical integration’ including
  - Contextual – BASIS protocol
  - Behavioural – AOSI
  - Brain function – EEG, ERP, Attention, Eye Tracking
  - Genetics – Buccal DNA
- Baseline 7-9 months; endpoint 14-15 months; follow up 2 and 3 years

At-risk sibling studies - summary

- Early behavioural indicators identified
  - Mostly early (non-verbal) social communication behaviours
  - Some motor and stereotyped behaviours
- Some surprising findings
  - Differences have not emerged before 12m
  - Early ‘engagement’ at 6m not atypical
- Neural responses vs. behavioural manifestations
- Different clinical vs. scientific approaches
  - BAP vs. identifying cases (outcome) approaches
Thank you!

Thanks to: My collaborators and the families in all our studies!

www.basisnetwork.org.uk