Identifying Infants Who Are At-Risk for Autism Spectrum Disorder

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Specific Aim: Identify infants who are at-risk for an eventual diagnosis of ASD

Why?

• Enable research on early ASD
• Develop early interventions
• Help families who have an atypical child
My Roles in this Project:

• Infant Development Psychologist
• Research Methodologist
• Parent Report Developer
• (Not an expert on ASD)

My Aim for Today:

• Describe the evolution of the First Year Inventory as an example of how to develop an effective measurement tool.
Parent Report Overview

- Parents provide the most extensive observational perspective.

- Parent report can work well (e.g., the MacArthur-Bates Communicative Development Inventory – CDI).

- Parent perspective has objective and subjective components (e.g., Infant Intentionality Questionnaire – IIQ).

Why is it difficult to identify infants who are at-risk for ASD?

- Most formal diagnostic criteria for ASD emerge after infancy so this is a probabilistic designation at best, and we don’t know exactly what we are looking for.

- Most atypical behaviors in infants could indicate various developmental disabilities.

- Atypical behaviors in infants are likely to be dimensional extremes of typical behaviors (e.g., emerges late or occurs either too frequently or too infrequently).

- Many parents don’t recognize these behaviors as atypical and medical practitioners don’t have enough contact to see them.
Steps Toward Creating the First Year Inventory

1. Assemble a cordial research team with broad expertise.
2. Examine relevant data in studies based on retrospective video analyses, parent report, clinical chart review, individual case studies, & sibling studies.
3. Organize relevant behaviors into categories.
5. Gather feedback on questions from experts and parents.
6. Gather small normative samples (n=\sim100) to estimate distribution of answers.
7. Revise questions (again and again!) until at least one answer is highly unlikely.
8. [In retrospect] Develop a scoring algorithm and file an official “Report of Invention”.
The First Year Inventory (FYI) Version 2.0

- Background information
- 46 items: “never,” “seldom,” “sometimes,” or “often”
- 14 multiple choice items
- 1 item on sound production
- 2 open-ended questions regarding concerns & unusual physical or medical characteristics
Sample Questions

**Orienting:** Does your baby turn to look at you when you call your baby’s name?

**Sensory:** Does your baby enjoy rubbing or scratching toys or objects for a long period of time?

**Affect:** Is it easy to understand your baby’s facial expressions?

**Imitation:** Does your baby copy or imitate your actions, like sticking out your tongue, clapping your hands, or shaking your head?

**Communication:** Does your baby communicate with you by using his or her finger to point at objects or pictures?

**Play:** Does your baby seem to get stuck on playing with a part of a toy (such as an eyeball, label, wheel or tag), instead of the whole toy?
Normative Study: (Reznick, et al., JADD, 2007)

- Return rate of 25% (1496 infants)
- Exclude preterm birth or late FYI completion
- Assemble usable data on 1300 infants
- Develop an algorithm for calculating risk
Algorithm for Scoring Risk

• Use norms for each question to identify unlikely answers and assign risk points: 1 risk point for least frequent response, 2\(^{nd}\) risk point if < 5%.

• Summing risk points reflected distribution of questions.

• Factor analysis and “construct shaping” yields:
  • Social-Communication Domain
    • Social Orienting & Receptive Communication
    • Social-Affective Engagement
  • Imitation
  • Expressive Communication
  • Sensory-Regulatory Domain
    • Sensory Processing
    • Regulatory Patterns
    • Reactivity
    • Repetitive Behavior
Scoring risk, con’t.

- Equate the weights of the 8 constructs by converting each construct to a score between 0-50.
- Focus differentiation on higher scores:
  - 50th percentile=10
  - 75th percentile=13
  - 90th percentile=20
  - 95th percentile=30
  - 98th percentile=40
- Compute average across constructs to get overall risk score, specific domain scores, and construct scores.
- Use normative data to establish probabilistic cut points for risk score and domain scores.
Methodology Moment

• A reflective construct is based on a set of correlated variables (e.g., safe road conditions defined by level pavement, clear lines, wide shoulder, few curves, etc.).

• A formative construct is based on the presence of various relevant variables (e.g., risk of wreck defined by road conditions, driver awareness, functional vehicle, traffic conditions, etc.).

• Risk for ASD is more formative, and this affects statistical approaches (e.g., item response theory (IRT) can be problematic).
Another Methodology Moment

- Sensitivity – proportion of infants with ASD (eventually) who are classified “at-risk”.
- Specificity – proportion of infants who do not have ASD (eventually) who are classified as “normal”.

- Perfect predictor: 100% sensitive and 100% specific.
- False positive: Classified “at risk” but no ASD
- False negative: Classified “normal” but with ASD

- A diagnostic tool must avoid false positives.
- A research tool is more concerned about false negatives.
Distribution of FYI Risk Scores

90%  95%  96%  97%  98%  99%
FYI-Retrospective Study: (Watson et al., JADD, 2007)

- Adapted FYI to ask for retrospective responses about child at 12 months
- Recruited parents of preschoolers
  - Sample: ASD (38); TYP (40); DD (15)
- Results:
  
  ASD > DD > TYP
  
  (F=127.96,
  M=28, 21, 3)
Risk Score Distribution of ASD Risk Scores by Group

- 99th percentile
- 98th percentile
- 90th percentile
- 95th percentile
FYI Follow-up: (Turner-Brown et al., 2013)

Obtain parent report of behavioral problems for 699 3-year-olds from normative study.

Conduct lab assessment of risk group and control group (n=38 + 5) using various clinical tools.

We find that 9 infants from the original sample have a definitive diagnosis of ASD.

What were their scores on the FYI?
<table>
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<tr>
<th>ASD Case</th>
<th>FYI Risk percentile</th>
<th>Social-Communication Total</th>
<th>Sensory-Regulatory Total</th>
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</table>

½ of infants with ASD at 3 years were high risk on FYI at 12 months.

1/3 of infants with a high FYI risk score at 12 months have a diagnosis of ASD by 3 years. 85% have DD or concern.
$\frac{1}{2}$ of infants with ASD at 7 years were high risk on FYI at 12 months.

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<th>soc_com</th>
<th>sen_reg</th>
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Additional Projects Using the FYI:

- EDP-1 & EDP-2 (Early Development Project) have used FYIs from 9756 families to recruit participants in the study of an intervention.

- IBIS (Infant Brain Imaging Study) has used the FYI to identify the highest risk siblings of children with ASD.
Another Methodology Moment

• Issues to consider in research with infants who have older siblings with ASD vs. infants who are at-risk for ASD
  • Yield of eventual ASD diagnosis
  • Parenting experience
  • Presence of older sibling with ASD
  • Genetics?
  • Other correlations?
Additional Projects Using the FYI:

- EDP-1 & EDP-2 (Early Development Project) have used FYIs from 9756 families to recruit participants in the study of an intervention.
- IBIS (Infant Brain Imaging Study) has used the FYI to identify the highest risk siblings of children with ASD.
- AOSI (Autism Observation Scale for Infants) study has clinical diagnoses of siblings at 36 months.
- A study at Yale has collected FYIs from siblings and conducted clinical diagnosis at 24 and 36 months.
42% of infants with ASD at 3 years were high risk on FYI at 12 months.
Steps Toward Creating FYI 3.1

1. Obtain funding from the Autism Speaks Foundation.

2. Review original questions and make modifications.

3. Do extensive review of recent relevant data, organize relevant behaviors into categories, and compose new questions.

4. Increase age range (8-15 months) and response range. It is now called the First Years Inventory.

5. Collaborate with designer (Purple Zante) and printer (Classic) to create attractive and functional materials.

6. Recruit cohort, follow-up at 2 and 3 years.

7. Develop scoring algorithm based on participants who have ASD.
Outer Envelope

North Carolina Child Development Survey

UNC Chapel Hill
PO Box 9798
Chapel Hill, NC 27515

Join families across the State!
Participate in the North Carolina Child Development Survey and help us help all families!
North Carolina Child Development Survey

Dear Parents:

Your family is invited to participate in the North Carolina Child Development Survey (NCCDS). We have contacted you after obtaining your name from birth certificates on file at the North Carolina State Center for Health Statistics. You will be one of approximately 36,000 families in North Carolina who are invited to participate in this survey! The goal of this project is to use parent responses to help identify children who are at-risk for later developmental problems such as autism spectrum disorder. Early detection will allow early treatment, and hopefully, better outcomes. Join families across North Carolina in helping us help all families!

Your initial participation will involve completing a brief survey called the First Years Inventory (FYI). Subsequent participation will involve completing brief surveys when your child is 2 and 3 years old. The FYI survey asks about your child's current typical behaviors indicating questions like how your child plays, expresses emotions, adapts to change, etc. Children display a wide range of behaviors and each child is unique. The FYI survey explores the range of typical behaviors for characteristics of young children that will help us identify early behaviors that can predict later problems. The short surveys at 2 and 3 years will ask about any problems that have emerged. If the surveys sent when your child is 2 and 3 years old indicate any risks that you are not aware of, we will contact you with information about steps you can take to have your child tested. Participating in the NCCDS through your survey responses is vitally important for helping us attain the goal of identifying children who are at-risk for later problems.

Please review all of the materials contained in your NCCDS packet. The instructions describe how to complete the FYI survey online or on paper, and it also contains important sections on confidentiality, risks, benefits, and contact information. Please note the Participant ID below carefully and follow instructions for entering it when you complete the FYI survey, either online or on paper. Your Participant ID is very important because it will let us link your survey to relevant information in your child's birth record.

B###

If you have any questions or concerns about this study, please visit our website (www.nccds.org), call the NCCDS Hotline at 919-525-1171, contact Dr. Steven Reznick at (919) 962-9720 or director@nccds.org, or the UNC CH Institutional Review Board at (919) 966-3113 or IRB_subjects@unc.edu.

Sincerely,
The NC Child Development Survey Team:
Dr. J. Steven Reznick, Dr. Grace Baranek,
Dr. Lauren Turner Brown, Dr. Elizabeth Craig,
Dr. Linda Watson and P. Kerry Bowser
Tri-fold – top page

First Years Inventory

North Carolina Child Development Survey
nccds.org

Welcome to the North Carolina Child Development Survey (NCCDS).
Join families across the state by completing the First Years Inventory (FYI). Your participation in this survey is our first step in learning more about building healthy families! We are interested in the behaviors that make your child unique. There are no right or wrong answers to these questions; they are simply descriptions of the range of behaviors that occur. Please answer every question with the most accurate answer that applies to your child at the present time.

Let’s get started! Participate in this first step of the NCCDS:
1) Turn to the first page and fill in responses for Section 1: Project Participation Information form.
2) Complete the FYI survey questions in Section 2 & 3.
Section 1  Project Participation Information

By submitting the FYI survey, you are granting your permission for us to contact you again with opportunities to participate in the next steps of this project over time. To make sure that we are able to contact you, please provide the information requested below. Please note that all follow-up contact will be directly related to the NC Child Development Survey.

PLEASE PRINT CLEARLY USING A BLACK OR DARK BLUE PEN, OR #2 PENCIL.

Date: mm / dd / yyyy

The person or persons filling out this form:

☐ Mother  ☐ Father  ☐ Other (specify):

Birth order: This child is ______ of ______ children born to this mother. (For example: 3rd of 3 children)

If the mother has more than 1 child, the date of her most recent previous birth was: mm / dd / yyyy

Mother’s first name:   Mother’s last name:
Father’s first name:   Father’s last name:
Child’s first name:   Child’s last name:
Child’s date of birth: mm / dd / yyyy
Family’s home/land line phone: ( )
Mother’s mobile phone: ( )   Mother’s work phone: ( )
Mother’s email address:
Father’s mobile phone: ( )   Father’s work phone: ( )
Father’s email address:

Please list two friends or relatives who we could contact if we are unable to reach you:

Name of friend/relative #1:   Name of friend/relative #2:
Relationship to your family:   Relationship to your family:
Land line phone number: ( )   Land line phone number: ( )
Mobile phone number: ( )   Mobile phone number: ( )
Work phone number: ( )   Work phone number: ( )
Email address:   Email address:
Section 2

First Years Inventory

For the following questions, please fill in the ONE ANSWER that best describes how frequently each behavior occurs.

Correct: completely fill in circle with black/blue pen or #2 pencil
Incorrect: place an “x” or a check mark in the circle

1. When you call your child’s name, does your child quickly look towards you?

2. Does your child get upset when you change a small part of his/her routine?

3. Does your child have trouble moving his/her body out of some positions (that is, gets stuck in a position)?

4. If you say to your child “Where is ___?” and you name a familiar person or object without pointing or showing, does he/she look at the person or object named?

5. Does your child stop what he/she is doing when you say “no” or “stop”?

6. Does your child appear very nervous if you lift him/her gently into the air above your head?

7. Does your child do any unusual activity over and over, such as twirling his/her hair?

8. Does your child easily accept being held by a stranger?

9. Does your child look at toys in unusual ways (for example, stare, look with his/her head sideways, or look from the corner of his/her eyes)?

10. Does your child use the first finger and tip of the thumb to pick up a very small object like a raisin or a Cheerio?

11. Does your child try to communicate with you by using his/her finger to point at things?

12. Does your child use gestures such as shaking his/her head, waving good bye, or raising his/her arms to be picked up?

13. Does your child seem overly sensitive to pain?

14. Does your child watch people’s faces when they are talking to each other?

15. Does your child clap his/her hands when other people are clapping?

16. Does your child prefer to play with just one part of a toy (for example, the wheel of a car or the eye of a doll) instead of the whole toy?

17. Does your child copy or imitate your actions when you do something silly with a toy or object like hugging a rattle or tapping a spoon on your head?
1. When you call your child's name, does your child quickly look towards you?  
   - Never 
   - Sometimes 
   - Always 

2. Does your child get upset when you change a small part of his/her routine?  
   - Never 
   - Sometimes 
   - Always 

3. Does your child have trouble moving his/her body out of some positions (that is, gets stuck in a position)?  
   - Never 
   - Sometimes 
   - Always 

4. If you say to your child "Where is ___?" and you name a familiar person or object without pointing or showing, does he/she look at the person or object named?  
   - Never 
   - Sometimes 
   - Always
Follow-up Postcard

Thank you for helping us take our first steps...

North Carolina Child Development Survey

Thank you for participating!

By submitting the survey you received from the NC Child Development Survey (NCCDS), your participation helps us learn about how children develop. Together with families across the state, you are an important building block in the NCCDS.

If you have not yet submitted your survey, there is still time to be a part of the NCCDS! We sent you a packet last week that described the NCCDS and included a survey about your child. You can mail the survey back to us now or complete the survey online at www.nccds.org. Thank you!!

P.S. – Your Participant ID is in your packet and also on this postcard (above your address).
Welcome to the NCCDS website!

Participate with families across the state in the first steps of the North Carolina Child Development Survey (NCCDS)!

Join families across North Carolina in helping us help all families! Your family may have received a packet in the mail from us if a birth certificate on file at the NC State Center for Health Statistics indicates that you gave birth to an infant within the age range we are interested in. If so, we encourage you to participate in this project through submitting the “First Years Inventory” (FYI) survey – either the paper survey in your packet or online version.

Your responses from the building blocks towards the goal of the NC Child Development Survey. Your responses to the FYI survey will enable us to learn about your infant. We are not saying that your infant is having any problems or is at-risk for problems in the future. But, by participating now and in our follow-up surveys, you will assist us in developing a way to identify children who are at-risk for later developmental problems such as Autism Spectrum Disorder (ASD). Early detection will allow early treatment, and hopefully, better outcomes.

Ready to begin the FYI online survey? (Click the blocks!)
• Mail 42,000 surveys to 94 counties mid-April 2012.
• Expect at least 10,000 responses.
• Receive 4,000 responses
What went wrong?
Constraints: 89 questions, lots of cooks, IRB, design.

Solution: 4-page folder & 6-page questionnaire; Versions A & B with 55 questions (21 are core).

Less is more, but constraints are constraints!
N.C. Politics, May 2012!

Coincidentally, “Help NC families” is the slogan for participating in NCCDS and for supporting gay marriage by voting against Amendment One.

Many of the 61% who voted for Amendment One may have viewed the NCCDS “Help NC families” mailing as anti-Amendment One, and thus they did not open it.
Steps Toward Creating FYI 3.2 and Cohort 2

1. The Autism Speaks Foundation allowed us to revise our plan for spending the remaining funds.

2. Cohort 1 viewed as pilot data. Contacted before 2\textsuperscript{nd} birthday with the MCHAT-R (Modified Checklist for Autism in Toddlers – Revised) and will be contacted again before 3\textsuperscript{rd} birthday.

3. We shifted the target age range to be 9-16 months.

4. We are using outcome data and Cohort 1 data to improve some questions, delete some questions, and change multiple-choice questions to dimensional questions.
Steps Toward Creating FYI 3.2 and Cohort 2

5. We will recruit Cohort 2 using a new strategy:
   • Send a postcard inviting online participation and showing a picture of the envelop they may receive.
   • Families who do not participate online will receive an h-mail with FYI 3.2.
   • Single survey (vs. longitudinal project), so h-mail will be a bi-fold with fewer questions and much less information.
   • Include an incentive or contact more families? [50x100=5x1000]

6. When Cohort 2 has been recruited, we will seek subsequent funding for a well defined follow-up based on Cohort 1.

7. We will develop an efficient and accurate algorithm for identifying 9-16 month-old infants who are at-risk for Autism Spectrum Disorder.
Things to Keep in Mind When Developing a Parent-Report Screening Tool

- Ask about specific behaviors rather than comparisons.
- Set appropriate balance of sensitivity vs. specificity.
- Carefully craft questions (and get lots of feedback):
  - Avoid figures of speech, idioms, examples, etc. that are unclear.
  - Avoid words that are difficult to translate.
  - Align questions with response dimensions.
- Develop possible scoring procedures using virtual data.
- Send pilot mailings.
• Please send me your comments/suggestions/questions

• reznick@unc.edu

• Thanks!