MINIMALLY VERBAL ASD: FROM BASIC MECHANISMS TO INNOVATIVE INTERVENTIONS

Helen Tager-Flusberg, Ph.D.
Boston University

IACC Meeting: April 9, 2013
Minimally Verbal Individuals with ASD

Why do they fail to acquire spoken language?

- We know almost nothing about these children and adolescents
- No theories to explain failure to acquire spoken language
- Dearth of novel treatments
Key Goals

1. Advance knowledge of the heterogeneous phenotypes associated with MV ASD
2. Develop and disseminate novel methods for assessing cognition, language and behavior
3. Propose and evaluate several mechanisms related to neural circuitry to explain why spoken language is not acquired
4. Complete randomized controlled trials of a novel intervention specifically designed for this population
5. Develop neural markers that predict response to intervention and that serve as measures of outcome success
Conceptual Framework

- Deficits in speech and language are related to impairments in neural connectivity

- Test several hypotheses about specific neurocognitive mechanisms that underlie speech/language deficits in this population

- Potential mechanisms to be tested in the context of the intervention study - explore developmental plasticity in children
Organization of BU ACE

- PI: Tager-Flusberg
- Core A: Administration and Data Management
  - Core B: Training/Education
    - Project I: Intervention
      - Schlau (BIDMC)
    - Project II: Speech Mechanisms
      - Guenther Manoach (MGH)
    - Project III: Auditory Perception
      - Shinn-Cunningham
  - Core C: Clinical
    - Joseph
    - Tager-Flusberg
Project I: Intervention

PI: Gottfried Schlaug MD (BIDMC)

Auditory-Motor Mapping Training (AMMT)

- Based on interventions developed for nonfluent aphasic patients (MIT)
- Trains association between sounds and articulatory actions to facilitate speech output
- Combined intonation (song) and use of pair of tuned drums to facilitate auditory-motor mapping
- Engaging: draws on relative strengths of children with ASD and enjoyable activities
- Delivered in structured (ABA), socially engaging context
Potential Critical Components

1. **Intonation** – singing engages bilateral frontal-temporal network (bias to right hemisphere); slowed presentation rate; phonemes isolated and therefore easier to process

2. **Imitation** – through repetitive training

3. **Hand-motor activities** – tapping drums while intonating words; may engage a sensori-motor network that controls both hands and articulatory activities

Wan et al. (2011) PLoS One
Child with therapist
6 Non-verbal children 5-9 years old
Randomized Control Trials of AMMT

**Study 1a**
- 40 children (5-10 years old): 20 AMMT and 20 Control therapy
- Baseline – 25 sessions (5 days/week; 45 minutes) – outcome assessment

**Study 1b** – Dosage effects
- 40 children: 20 High frequency (5 days/week); 20 Low frequency (3 days/week)
- Baseline – 25 sessions - outcome
Training trials

- 15 picture symbols (words, phrases) – training items
  - Listen – therapist intonates target word/phrase
  - Unison production – ‘let’s sing together’
  - Partially supported production – therapist fades out
  - Immediate repetition – therapist followed by child’s turn
  - Own production – child intones phrase on own

Control therapy – no ‘singing or drums’

Outcome measures:
1. Production of trained and untrained items
2. LENA in home for 24 hours
Predictors of response to treatment

1. Behavioral and cognitive measures, drawn from Core assessment (e.g., nonverbal IQ; measures of joint attention; speech praxis)
2. Structural and functional neural connectivity measures
   - Focus on arcuate fasciculus (DTI) – atypical asymmetry
   - fcMRI between frontal and temporal cortical language regions
Arcuate fasciculus volumes

![Graph showing volume comparison between minimally verbal ASD and typically-developing individuals.](image)

- **Volume in mm³**
  - **Left**
  - **Right**

- **Minimally verbal ASD**
- **Typically-developing**

![Brain images comparing ASD and Ctrl individuals.](image)
MPI: Frank Guenther & Dara Manoach (MGH)

DIVA/GODIVA Model

- Most comprehensive neurocomputational model of speech production
- Requires integration of auditory, somatosensory, and motor information in the brain
- Speech sounds are learned – store auditory target, use auditory feedback control system to control production of sound in early repetitions
- Repeated productions lead to tuning feedforward commands, supplanting feedback-based control signals
Architecture of GODIVA
Gradient Order – Directions into Velocities of Articulators
Schematic Model

- **Left preSMA:** Metrical Sequencing
- **Left SMA:** Motor Program Triggering
- **Left IFS/BA 9:** Phonological Working Mem.
- **Left vPMC:** Syllable Motor Programs
- **Bilateral pSTg, aSMg:** Auditory & Somatosensory Error Maps
- **Bilateral MC:** Articulator Pos. & Velocity Maps
- **Right vPMC:** Feedback Control Map

**Legend:**
- **DIVA**
- **GODIVA**
- **Impaired in ASD**
Speech in ASD

• **Primary hypothesis:** deficits in speech production are related to abnormalities in white matter integrity and reduced coordination of activity in the speech network – specifically in the pathway between left SMA (supplementary motor area) and left vPMC (ventral premotor cortex)

• Pathway is critical to initiation of speech output
ACE Studies

**Study 1**
Children from intervention study (expect ~50% participation). Pre/post AMMT intervention
- Anatomical scan
- fcMRI (resting state)
- DTI

**Study 2**
Adolescents/young adults – from intact language to minimally verbal (N=75) and age/sex matched controls
Pilot data

Lower FA
In ASD –
vPMC diffs

A: ~200 controls (resting state fcMRI); B: ASD participant
Project III
Auditory Processing

PI: Barbara Shinn-Cunningham

Organizing auditory environment

- Auditory processing involves segregating input into meaningful units (or ‘objects’)
- Deficits in auditory scene analysis, resulting from abnormalities in structural and functional connectivity underlie speech and language impairments
**Auditory scene segregation**

*Fig. 1 Impact of grouping on perception.* When grouping fails (left), individual objects (words) are difficult to interpret; instead, the entire scene is processed as one mass, making it difficult to extract **word meaning**. When the scene is segregated properly (right), **word meaning** is easier to decipher, but we are forced to process the scene serially, word by word. (Figure adapted from [15].)
ACE Studies

**Study 1**
Children from intervention study (expect ~50% participation). Pre/post AMMT intervention
- ERP to detect perceptual organization with tones and speech;
- ERP to detect changes in frequency and intensity for tones and speech
- EEG neural oscillations (linked to scene analysis and selective attention)

**Study 2**
Adolescents/young adults – from intact language to minimally verbal (N=75) and age/sex matched controls
Example of experimental conditions

Perceptual Organization
ACE Core Units

A: Administration and Data Management
   BU ACE; Data Coordinating Center BU/SPH

B: Research Training and Education
   BU Students, Post-docs, staff activities
   External dissemination of research

C: Clinical
   Recruitment of families
   Comprehensive behavioral diagnosis and assessments
   Novel assessment approaches (eye-tracking; psychophysiology)
   Pre/post evaluation of children in Study 1
Study 1 – Flow through projects

C = Core C
MRI = Project II
ERP = Project III
AMMT= Project I
Partnersing scientists and families

Creating an on-line community to maximize potential for success on this challenging research program

- **Research Collaboration Platform** –
  - Links all components of the ACE internally -
  - Links ACE projects to enrolled families
  - Access to video, scheduling, participant tracking systems
  - Training materials – remote web-based interactive multimedia instruction, feedback and evaluation
  - Communications systems – internal ‘teams’; project-family
  - File sharing
Thank You!

• Gottfried Schlaug; Catherine Wan (BIDMC)
• Frank Guenther; Jason Boland
• Dara Manoach; Randy Buckner (MGH)
• Barbara Shinn-Cunningham (CompNet)
• Elysse Sussman (AECOM)
• Robert Joseph
• Matthew Goodwin; Rupal Patel (NEU)
• Alice Bisbee; John Lu; Hanna Gerlovin; Sharon Coleman (DCC: BU/SPH)

Students and staff at BU ROADD
Families investing in our ACE dreams