BOSTON UNIVERSITY

MINIMALLY VERBAL ASD: FROM *BASIC MECHANISMS* TO *INNOVATIVE INTERVENTIONS*

Helen Tager-Flusberg, Ph.D.
Boston University

IACC Meeting: April 9, 2013

Boston University: ACE

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

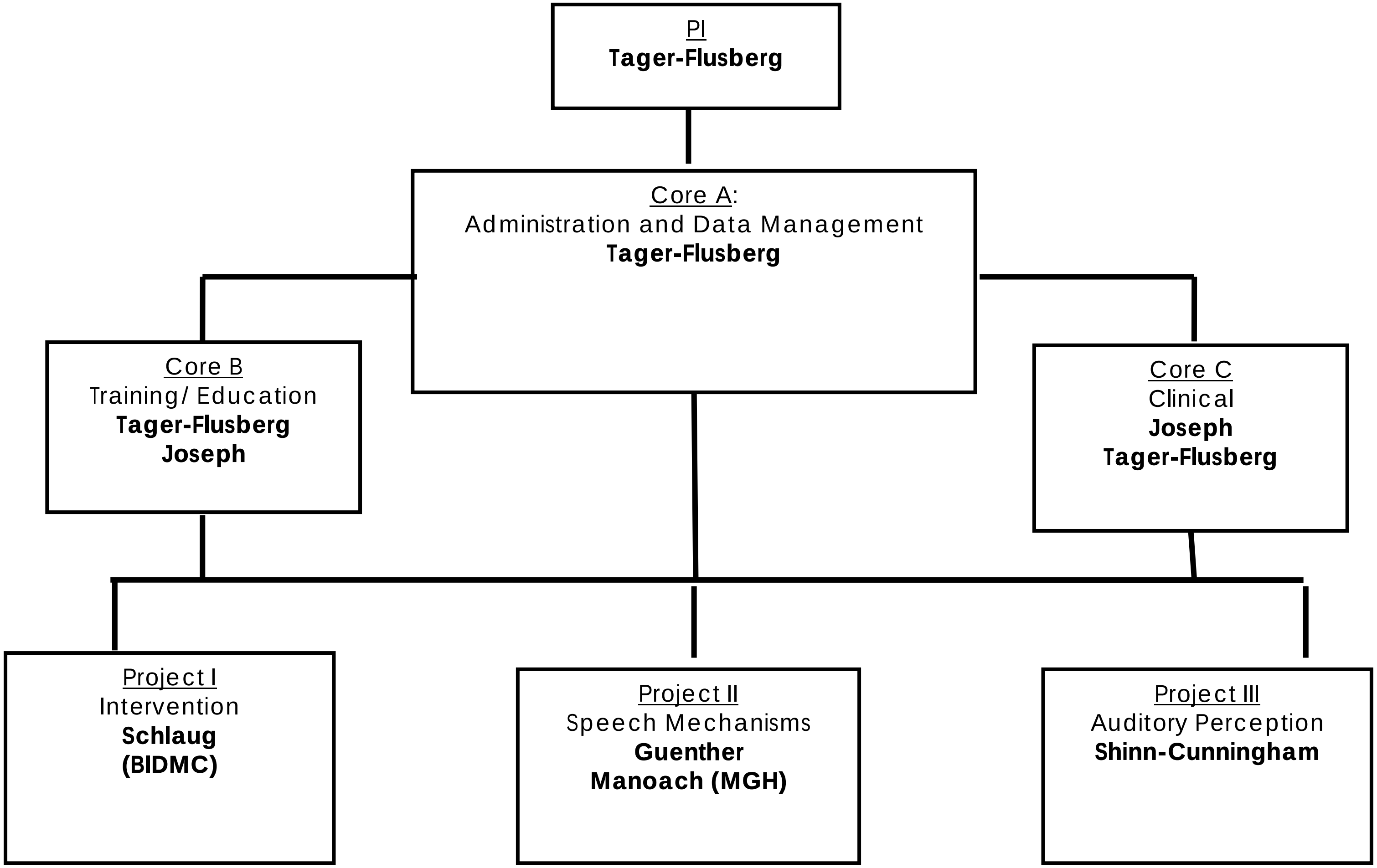
Key Goals

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



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

AMMT

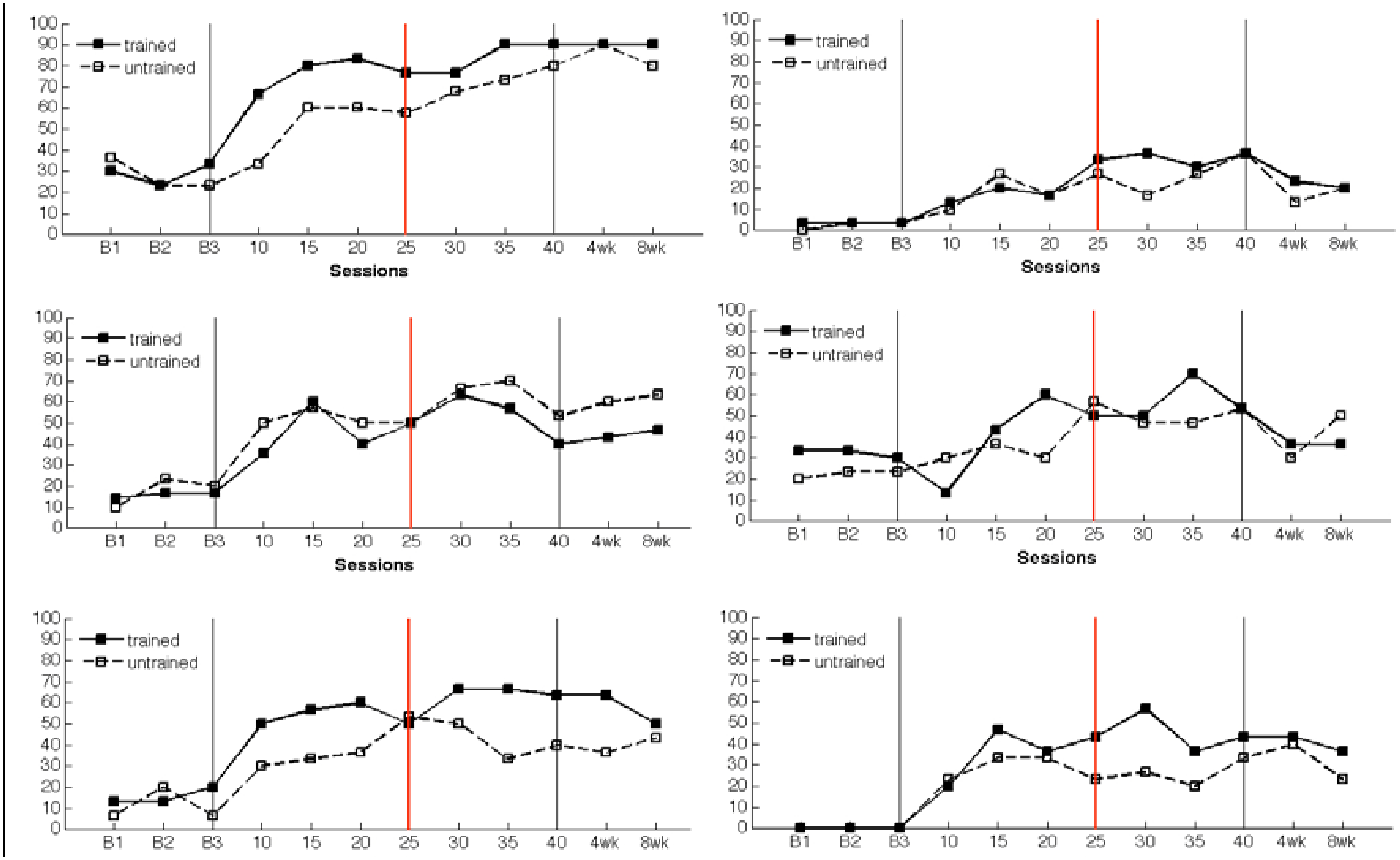
Potential Critical Components

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'

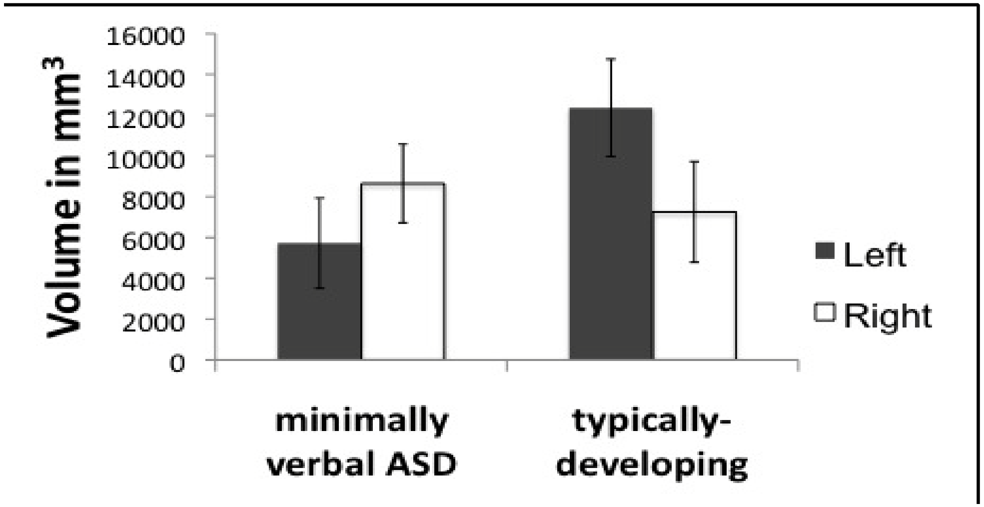
Outcome measures:

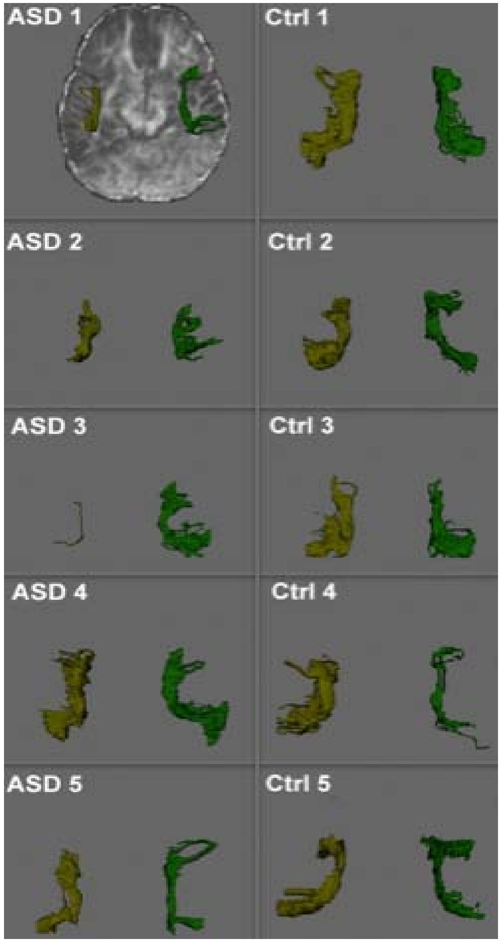
1. Production of trained and untrained items
2. LENA in home for 24 hours

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





Project II:
Speech Mechanisms

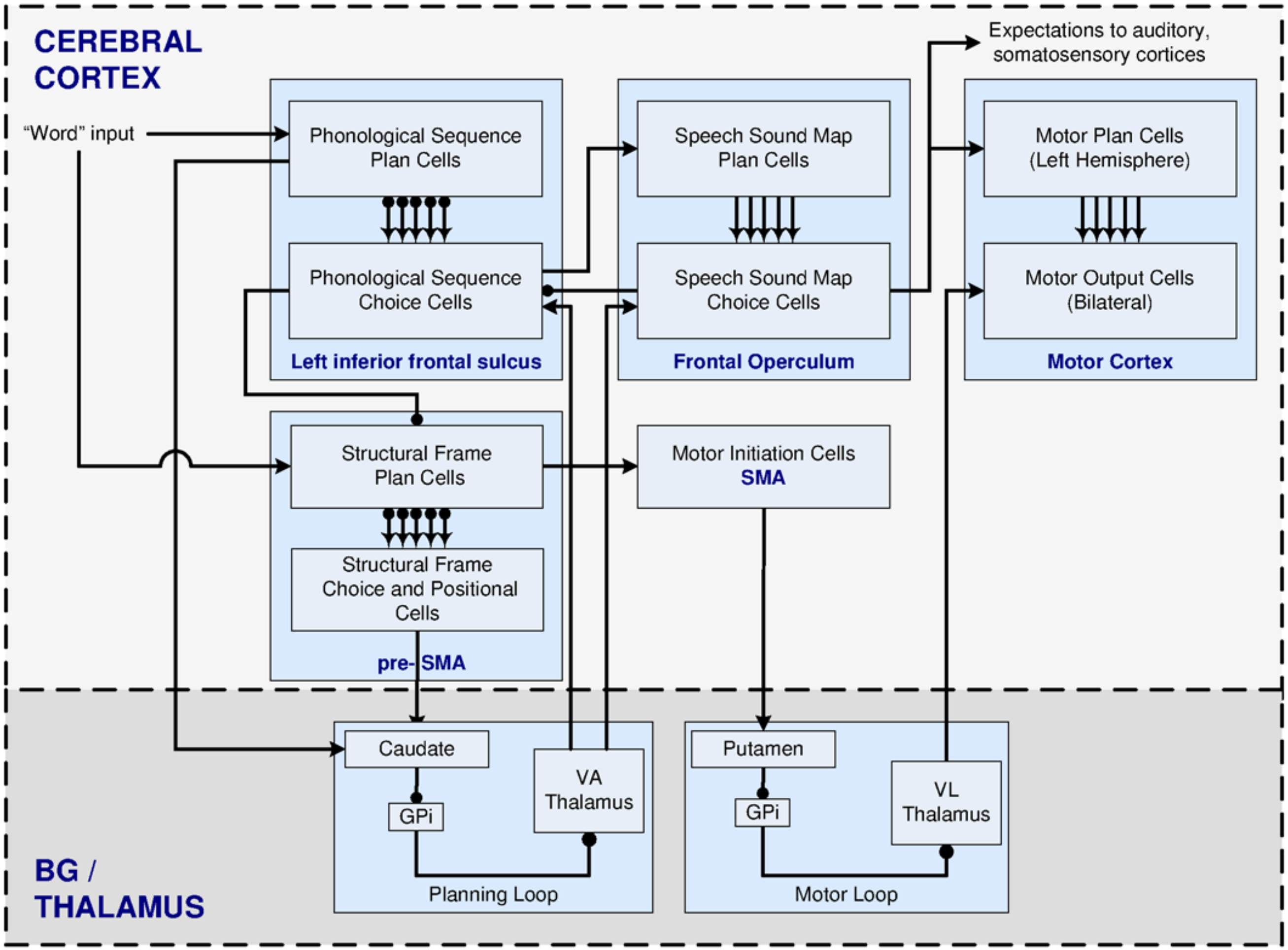
MPI: Frank Guenther & Dara Manoach (MGH)

<u>DIVA/GODIVA Model</u>

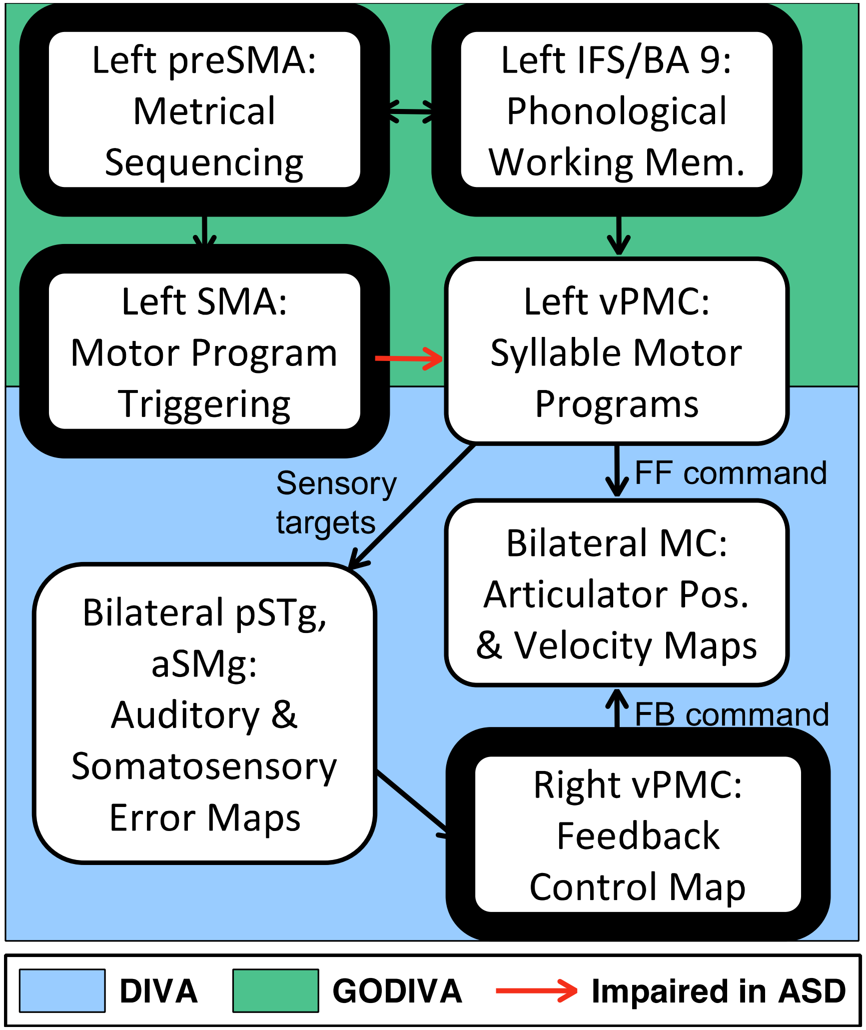
- Most comprehensive neurocomputational model of speech production
- Requires integration of auditory, somatosensory, and motor information in the brain
- Speech sounds are learned – store auditory target, use auditory feedback control system to control production of sound in early repetitions
- Repeated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

Architecture of GODIVA

Gradient Order – Directions into Velocities of Articulators



Schematic Model



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

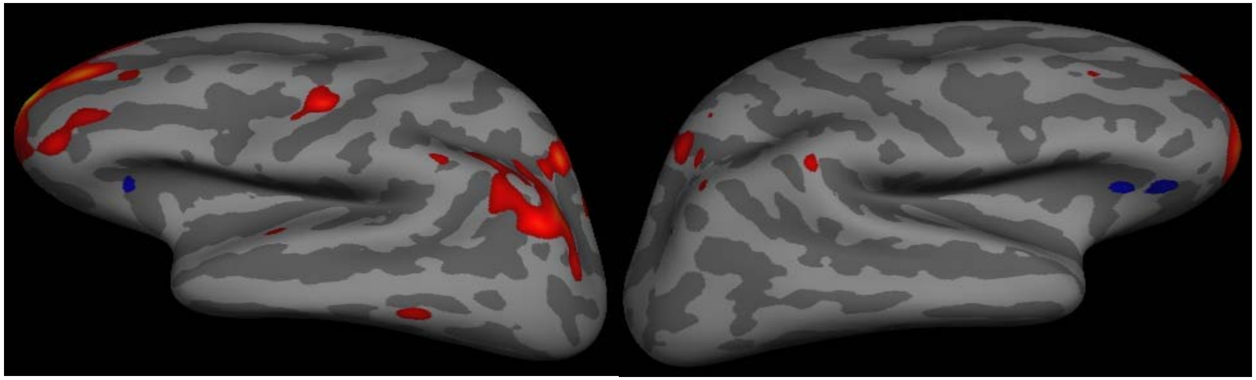
- Anatomical scan
- fcMRI (resting state)
- DTI

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

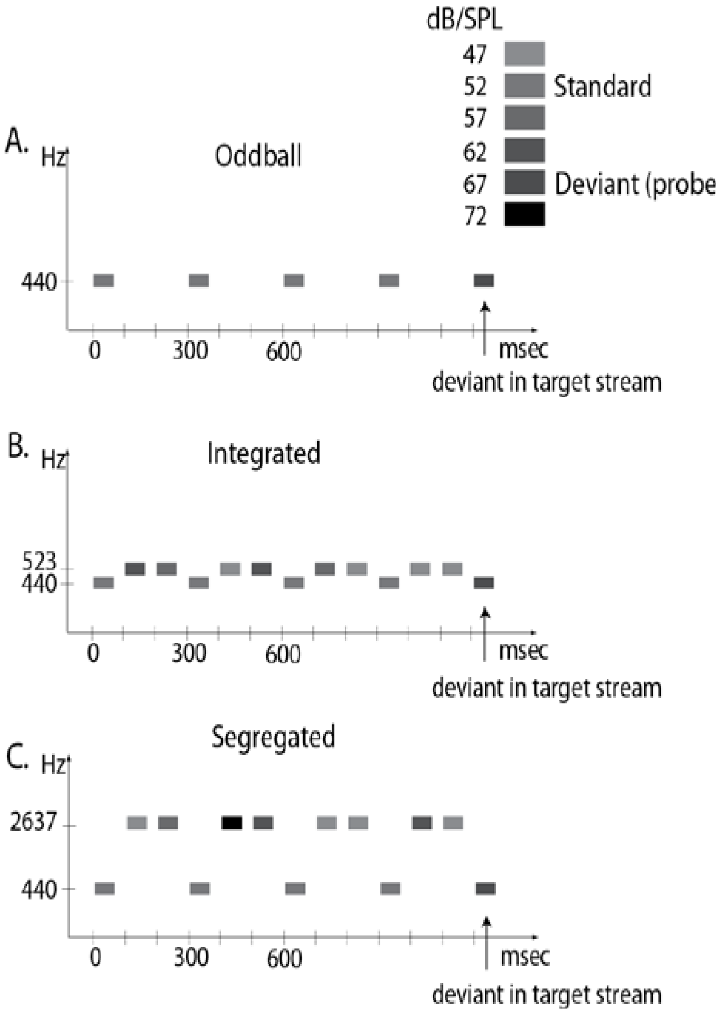
Children from intervention study (expect ~50% participation). Pre/post AMMT intervention

- 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

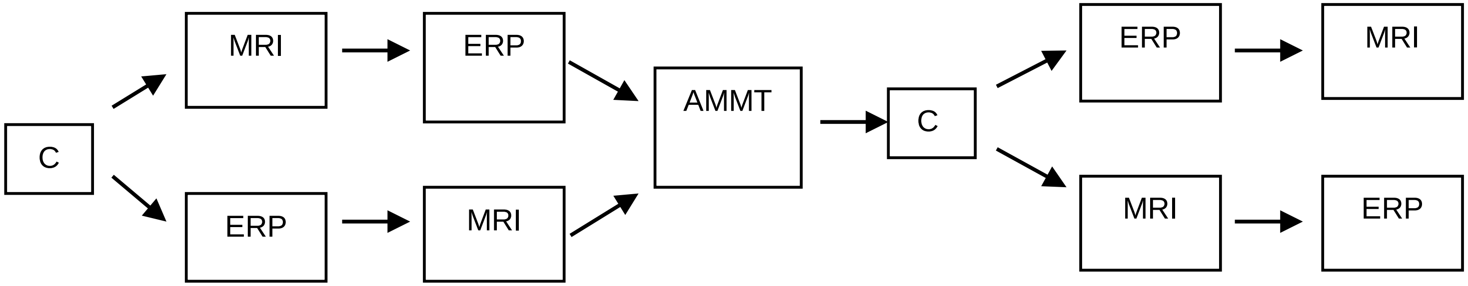
Recruitment of families

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

Partnering 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 multi-media 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