

# Diagnostic Markers of Childhood Apraxia of Speech

Lawrence D. Shriberg<sup>a</sup>

Kathy J. Jakielski<sup>b</sup>

Edythe A. Strand<sup>c</sup>

<sup>a</sup>Waisman Center  
University of Wisconsin-Madison

<sup>b</sup>Department of Communication Sciences and Disorders  
Augustana College

<sup>c</sup>Department of Neurology, Mayo Clinic-Rochester

American Speech-Language-Hearing Association  
National Convention, Philadelphia, PA  
November 18, 2010

Slide 1

## Disclosure Statement

We have no financial or non-financial interest in any organization whose products or services are described, reviewed, evaluated, or compared in the presentation.

Slide 2

## Acknowledgments

### Waisman Center Phonology Project University of Wisconsin-Madison

### Collaborators for Motor Speech Projects

Marios Fourakis	Jane McSweeney	Leonard Abbeduto	Jordan Green
Sheryl Hall	Alison Scheer-Cohen	Kirrie Ballard	Barbara Lewis
Heather Karlsson	Sonja Tatro	Adriane Baylis	Christopher Moore
Joan Kwiatkowski	Christie Tilkens	Stephen Camarata	Rhea Paul
Heather Lohmeier	David Wilson	Thomas Campbell	Nancy Potter
		Kathy Chapman	Sharynne McCleod
		Peter Flipsen, Jr.	Angela Morgan
Roger Brown	Gordana Raca	Morton Gernsbacher	Bruce Tomblin
David Dimmock	Gregory Rice	Hill Goldsmith	Erin Wilson
Craig Jackson	Shelley Smith		
Jennifer Laffin	Elizabeth Worthey		

### Biostatistics and Genomics

This research is supported by the National Institute on Deafness and Other Communication Disorders [DC00496], an American Recovery and Reinvestment Act Supplement Grant, and a core grant to the Waisman Center from the National Institute of Child Health and Development [HD03352].

Slide 3

## Diagnostic Markers of Childhood Apraxia of Speech

- I. **Rationale**
  - A. Genomic
  - B. Diagnostic
- II. **Methods**
  - A. Data Acquisition and Reduction
  - B. Analytic Framework
  - C. Methodological Constraints
- III. **Results**
  - A. Promising Diagnostic Markers
  - B. Group and Subgroup Comparisons
- IV. **Discussion**

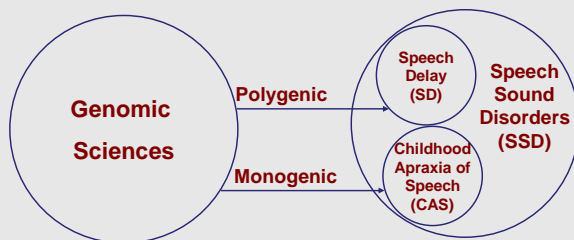
Slide 4

## Genomic Premise 1: The Genomic Origins of CAS Are Rare Single Polymorphisms

No.	Type	Subtype	Abbreviation	Risk Factors	Processes Affected
1	Speech Delay	Speech Delay-Genetic	SD-GEN	Polygenic/ Environmental	Cognitive-Linguistic
2		Speech Delay- Otitis Media with Effusion	SD-OME	Polygenic/ Environmental	Auditory-Perceptual
3		Speech Delay- Developmental Psychosocial Involvement	SD-DPI	Polygenic/ Environmental	Affective- Temperamental
4	Motor Speech Disorder	Motor Speech Disorder- Apraxia of Speech	MSD-AOS	Monogenic? Oligogenic?	Speech-Motor Control
5		Motor Speech Disorder- Dysarthria	MSD-DYS	Monogenic? Oligogenic?	Speech-Motor Control
6		Motor Speech Disorder- Not Otherwise Specified	MSD-NOS	Monogenic? Polygenic? Oligogenic? Environmental?	Speech-Motor Control
7	Speech Errors	Speech Errors-Sibilants	SE-/s/	Environmental	Phonological Attunement
8		Speech Errors-Rhotics	SE-/r/	Environmental	Phonological Attunement

Slide 5

## Genomic Premise 2: The Genomic Origins of CAS Can Be Identified Using Current Sequencing and Bioinformatics Methods



Slide 6

## Genetic Research in CAS

- **FOXP2**
  - Studies reporting Speech Delay (Zhao et al., 2010)
  - Studies of downstream genes (Roll et al., 2010)
  - Studies with mammalian models (avian, murine, other)
- **FOXP1**
  - Carr et al. (2010); Hamdan et al. (2010)
  - Horn et al. (2010); Pariani (2010)
- **FOXP1**
  - Brunetti-Pierri et al. (2010)
- **ELP4**
  - Pal et al. (2010)
- **RAI1**
  - Kogan et al. (2010)
- Some recent literature reviews:
  - Bishop (2009); Grigorenko (2009); Lewis (2010); Newbury & Monaco (2010); Ramus & Fisher (2009); Shriberg (2010)

Slide 7

## Example of Phenotype Issues: Speech Sound Disorder? Severe Speech Delay? CAS?

Psychiatry and Clinical Neuroscience 2010; 64: 565-573 doi:10.1111/j.1440-1819.2010.02123.x

Regular Article

Association between *FOXP2* gene and speech sound disorder in Chinese population

Yunjing Zhao, MD,<sup>1</sup> Hongwei Ma, MD, PhD,<sup>1\*</sup> Yueping Wang, MD,<sup>2</sup> Hong Gao, BA,<sup>2</sup> Chunyan Xi, MD, PhD,<sup>3</sup> Tainyi Hua, MD, PhD,<sup>1</sup> Yaru Zhao, MD,<sup>1</sup> Guangrong Qiu, MD, PhD<sup>3</sup>

<sup>1</sup>Department of Developmental Pediatrics, Shengjing Hospital, <sup>2</sup>Central Laboratory of Shengjing Hospital, and <sup>3</sup>Department of Medical Genetics, China Medical University, Shenyang, China

**Aim:** *FOXP2* was described as the first gene relevant to human speech and language disorders. The main objective of this study was to compare the distribution of *FOXP2* gene polymorphisms between patients with speech sound disorder and healthy controls.

**Methods:** Five *FOXP2* polymorphisms, rs23875, rs2396722, rs1852469, rs17137124 and rs1456031, were analyzed in 150 patients with speech sound disorder according to DSM-IV, as well as in 140 healthy controls. Coding exons for key domains of *FOXP2* were also sequenced in all the patients.

**Results:** Significant differences in the genotype ( $P=0.001$ ) and allele ( $P=0.0025$ ) frequencies of rs1852469 (located 5' upstream of the ATG initiation codon) were found between patients and controls. The excess of the T allele in the patients group remained significant after Bonferroni correction ( $P=0.0126$ ). Further investigations revealed a risk haplotype: rs2396722T/rs1852469T. Our screening of key domains did not detect any point mutations in this sample. But we detected heterozygous triplet deletion of the glutamine-encoding region of exon 3 that alter *FOXP2* protein sequence in five probands. These changes are predicted to yield a polyglutamine tract reduction from 40 to 39 consecutive glutamines.

**Conclusions:** Our data support a possible role of *FOXP2* in the vulnerability to speech sound disorder, which adds further evidence to implicate this gene in speech and language functions.

**Key words:** articulation disorder, DNA sequencing, *FOXP2* gene, haplotype analysis, single nucleotide polymorphism.

Slide 8

## Madison Genomic Research in Idiopathic CAS: Progress To Date

- **Ten families assessed to date**
  - Each family includes one or more nuclear members with Idiopathic CAS
  - Speech assessment using methods described in this presentation
- **Genomic analyses**
  - Array Comparative Genomic Hybridization (aCGH; copy number)
  - Exome Sequencing; Bioinformatics
- **Results to date**
  - aCGH
    - No replication of reported genes or regions of interest
    - No new gene or regions of interest
  - Bioinformatic analyses
    - No findings – Initiated November, 2010

Slide 9

## Diagnostic Markers of Childhood Apraxia of Speech

- I. **Rationale**
  - A. Genomic
  - B. Diagnostic
- II. **Methods**
  - A. Data Acquisition and Reduction
  - B. Analytic Framework
  - C. Methodological Constraints
- III. **Results**
  - A. Promising Diagnostic Markers
  - B. Group and Subgroup Comparisons
- IV. **Discussion**

Slide 10

## Diagnostic Premise 1: Phenotype Constraints Remain the Major Need in Genomic, Diagnostic, and Other CAS Research

Nearly a decade ago . . .

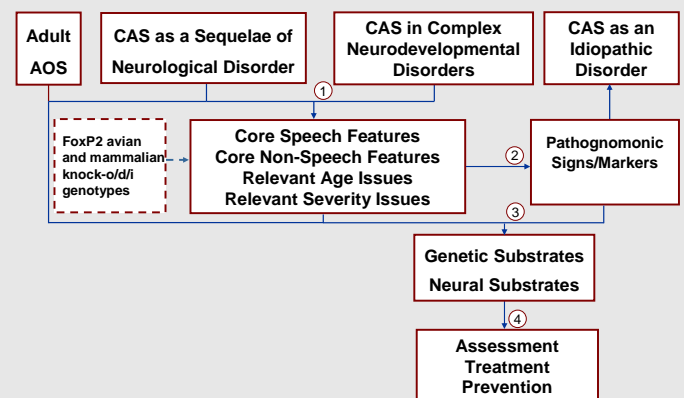
- "...lack of [a definition and] an agreed-upon set of criteria for subject selection [is the] single most important impediment to theoretical and clinical advancement in AOS."
 

McNeil (2001)
- "...the problem lies not so much in defining the underlying impairment of AOS as in a lack of clear operational definitions or procedural criteria for the differential diagnosis of AOS."
 

Maassen (2002)

Slide 11

## Diagnostic Premise 2: Identifying Markers of CAS in Neurologic and Neurodevelopment Contexts Will Inform Markers of Idiopathic CAS



Slide 12

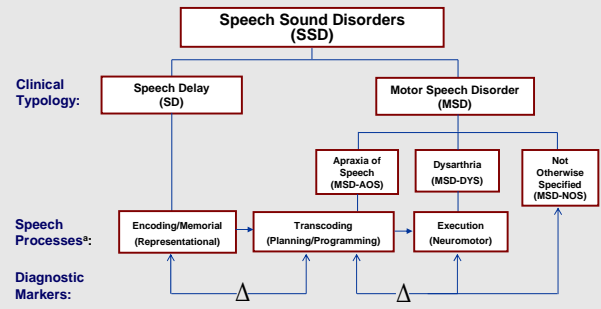
### Diagnostic Premise 3: Validated Behavioral Markers of CAS Will Inform Explanatory Accounts of CAS

What are the core perceptual and acoustic signatures of CAS

- ❑ in which linguistic domains?
- ❑ from which assessment tasks?
- ❑ in which neurologic, neurodevelopmental, and idiopathic contexts?
- ❑ at which cognitive/biological ages?

Slide 13

### Diagnostic Premise 4: A Conventional Three-Phase Speech Processing Perspective Provides a Sufficient Framework Toward an Explanatory Account of CAS



Sources: van der Merwe; Guenther; Levelt; others

Slide 14

### Diagnostic Markers of Childhood Apraxia of Speech

- I. Rationale
  - A. Genomic
  - B. Diagnostic
- II. **Methods**
  - A. **Data Acquisition and Reduction**
  - B. Analytic Framework
  - C. Methodological Constraints
- III. Results
  - A. Promising Diagnostic Markers
  - B. Group and Subgroup Comparisons
- IV. Discussion

Slide 15

### Methods: Five Participant Groups and Subgroups

Description	Acronym	n	Age (yrs)	Percentage of Consonants Correct (PCC)	
				$\bar{X}$	SD
Neurogenetic Apraxia of Speech	CAS-N	16	4 - 50		
Chromosome Translocation		3	11,12,16	77.0	5.8
FOXP2		1	4	42.6	
		3	18, 23, 50	88.3	2.4
Galactosemia		8	5 - 16	67.6	20.0
Joubert Syndrome		1	11	70.0	

Slide 16

### Methods: Five Participant Groups and Subgroups

Description	Acronym	n	Age (yrs)	Percentage of Consonants Correct (PCC)	
				$\bar{X}$	SD
Neurogenetic Apraxia of Speech	CAS-N	16	4 - 50		
Chromosome Translocation		3	11,12,16	77.0	5.8
FOXP2		1	4	42.6	
		3	18, 23, 50	88.3	2.4
Galactosemia		8	5 - 16	67.6	20.0
Joubert Syndrome		1	11	70.0	
Idiopathic Apraxia of Speech	CAS-I	16	5 - 19	71.9	12.4

Slide 17

### Methods: Five Participant Groups and Subgroups

Description	Acronym	n	Age (yrs)	Percentage of Consonants Correct (PCC)	
				$\bar{X}$	SD
Neurogenetic Apraxia of Speech	CAS-N	16	4 - 50		
Chromosome Translocation		3	11,12,16	77.0	5.8
FOXP2		1	4	42.6	
		3	18, 23, 50	88.3	2.4
Galactosemia		8	5 - 16	67.6	20.0
Joubert Syndrome		1	11	70.0	
Idiopathic Apraxia of Speech	CAS-I	16	5 - 19	71.9	12.4
Acquired Apraxia of Speech	AOS	3	45, 53, 67	92.4	4.5

Slide 18

## Methods: Five Participant Groups and Subgroups

Description	Group			Percentage of Consonants Correct (PCC)	
	Acronym	n	Age (yrs)	$\bar{X}$	SD
Neurogenetic Apraxia of Speech	CAS-N	16	4 - 50		
Chromosome Translocation		3	11,12,16	77.0	5.8
FOXP2		1	4	42.6	
Galactosemia		3	18, 23, 50	88.3	2.4
Joubert Syndrome		8	5 - 16	67.6	20.0
Joubert Syndrome		1	11	70.0	
Idiopathic Apraxia of Speech	CAS-I	16	5 - 19	71.9	12.4
Acquired Apraxia of Speech	AOS	3	45, 53, 67	92.4	4.5
Speech Delay	SD	16	3 - 6	64.3	13.4

Slide 19

## Methods: Five Participant Groups and Subgroups

Description	Group			Percentage of Consonants Correct (PCC)	
	Acronym	n	Age (yrs)	$\bar{X}$	SD
Neurogenetic Apraxia of Speech	CAS-N	16	4 - 50		
Chromosome Translocation		3	11,12,16	77.0	5.8
FOXP2		1	4	42.6	
Galactosemia		3	18, 23, 50	88.3	2.4
Joubert Syndrome		8	5 - 16	67.6	20.0
Joubert Syndrome		1	11	70.0	
Idiopathic Apraxia of Speech	CAS-I	16	5 - 19	71.9	12.4
Acquired Apraxia of Speech	AOS	3	45, 53, 67	92.4	4.5
Speech Delay	SD	16	3 - 6	64.3	13.4
Typically Speaking	TS	100	3 - 16	95.7	6.1

Slide 20

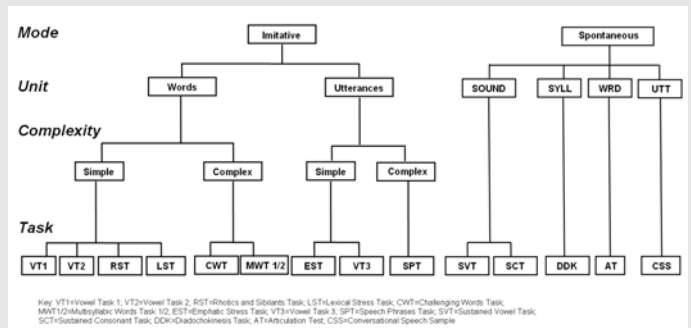
## Methods: Madison Speech Assessment Protocol (MSAP)<sup>a</sup>

- **Four age-based protocols:**  
Preschool, school-aged, adolescent, adult
- **Protocols include 15 tasks assessing speech, voice, and prosody**
  - Articulation Test
  - Challenging Phrase Task
  - Challenging Words Task
  - Consonant Tasks
  - Conversational Speech Sample
  - DDK Task
  - Nonword Repetition Tasks
  - Phonation Tasks
  - Stress Tasks
  - Vowel Tasks

<sup>a</sup>Shriberg et al. (2010)

Slide 21

## MSAP Task Hierarchy



Key: VT1=Vowel Task 1; VT2=Vowel Task 2; RST=Rhymes and Syllables Task; LST=Lexical Stress Task; CWT=Challenging Words Task; MW1/2=Multisyllabic Words Task 1/2; EST=Emphatic Stress Task; VT3=Vowel Task 3; SPT=Speech Phrases Task; SVT=Sustained Vowel Task; SCT=Sustained Consonant Task; DDK=Diadochokinesis Task; AT=Articulation Test; CSS=Conversational Speech Sample

Slide 22

## Sustained Vowel Task (SVT)

Trial	Vowel	Duration (in sec.)
1	/a/	_____
2	/a/	_____
3	/a/	_____

Slide 23

## Sustained Consonant Task (SCT)

Trial	Consonant	Duration (in sec.)
1	/h/	_____
2	/h/	_____
3	/h/	_____

Slide 24

**Vowel Task 1 (VT1)  
Corner Vowels**

- |         |         |          |          |
|---------|---------|----------|----------|
| 1. beet | 5. pot  | 9. bat   | 13. bat  |
| 2. bat  | 6. bat  | 10. beet | 14. pot  |
| 3. boot | 7. boot | 11. pot  | 15. boot |
| 4. beet | 8. pot  | 12. boot | 16. beet |

**Slide 25**

**Vowel Task 2 (VT2)  
Other Vowels & Diphthongs**

- |            |          |            |            |
|------------|----------|------------|------------|
| 1. putt    | 12. bite | 23. put    | 34. putt   |
| 2. bite    | 13. bit  | 24. bait   | 35. bought |
| 3. bought  | 14. boat | 25. Bert   | 36. bait   |
| 4. Bert    | 15. pet  | 26. boat   | 37. put    |
| 5. bit     | 16. pout | 27. bit    | 38. Bert   |
| 6. bait    | 17. bait | 28. boy    | 39. boat   |
| 7. pet     | 18. putt | 29. pet    | 40. boy    |
| 8. boat    | 19. boy  | 30. pout   | 41. putt   |
| 9. put     | 20. pet  | 31. bought | 42. put    |
| 10. boy    | 21. bite | 32. bite   | 43. Bert   |
| 11. bought | 22. pout | 33. bit    | 44. pout   |

**Slide 26**

**Vowel Task 3 (VT3)**

- |  |  |
|--|--|
| 1. She needs strawberry jam on her toast.  | 11. Did you like the zoo this spring?      |
| 2. He has a blue pen.                      | 12. I am tall.                             |
| 3. Did you like the zoo this spring?       | 13. Chuck seems thirsty after the race.    |
| 4. I am tall.                              | 14. Did you like the zoo this spring?      |
| 5. Chuck seems thirsty after the race.     | 15. He has a blue pen.                     |
| 6. He has a blue pen.                      | 16. Chuck seems thirsty after the race.    |
| 7. She needs strawberry jam on her toast.  | 17. I am tall.                             |
| 8. Did you like the zoo this spring?       | 18. She needs strawberry jam on her toast. |
| 9. I am tall.                              | 19. He has a blue pen.                     |
| 10. She needs strawberry jam on her toast. | 20. Chuck seems thirsty after the race.    |

**Slide 27**

**Rhotics and Sibilants Task**

- |          |           |           |           |           |
|----------|-----------|-----------|-----------|-----------|
| 1. sin   | 9. kiss   | 17. ride  | 25. spoon | 33. spoon |
| 2. crude | 10. spoon | 18. kiss  | 26. burr  | 34. sin   |
| 3. soon  | 11. skin  | 19. soon  | 27. soon  | 35. burr  |
| 4. bird  | 12. burg  | 20. burr  | 28. ride  | 36. crude |
| 5. skin  | 13. sin   | 21. skin  | 29. bird  | 37. bird  |
| 6. burr  | 14. crude | 22. crude | 30. kiss  | 38. soon  |
| 7. ride  | 15. bird  | 23. burg  | 31. skin  | 39. ride  |
| 8. burg  | 16. spoon | 24. sin   | 32. burg  | 40. kiss  |

**Slide 28**

**Challenging Words Task (CWT)**

- |                |               |
|----------------|---------------|
| 1. helicopter  | 7. alligator  |
| 2. kangaroo    | 8. watermelon |
| 3. elephant    | 9. stars      |
| 4. caterpillar | 10. skates    |
| 5. tomato      | 11. scissors  |
| 6. octopus     | 12. zipper    |

**Slide 29**

**Multisyllabic Words Task 1 (MWT1)**

- |                 |                      |
|-----------------|----------------------|
| 1. animal       | 14. associate        |
| 2. mobilize     | 15. symphony         |
| 3. catalog      | 16. enthusiasm       |
| 4. calendar     | 17. suspicious       |
| 5. syllable     | 18. skeptical        |
| 6. governor     | 19. bicyclist        |
| 7. navigator    | 20. orchestra        |
| 8. Colorado     | 21. substantial      |
| 9. permanent    | 22. susceptible      |
| 10. hemisphere  | 23. municipal        |
| 11. especially  | 24. specific         |
| 12. establish   | 25. Episcopal church |
| 13. consequence |                      |

**Slide 30**

## Multisyllabic Words Task 2 (MWT2)

- |                |                       |
|----------------|-----------------------|
| 1. emphasis    | 11. consciousness     |
| 2. probably    | 12. suspicious        |
| 3. sympathize  | 13. municipal         |
| 4. terminal    | 14. orchestra         |
| 5. synthesis   | 15. specific          |
| 6. especially  | 16. statistics        |
| 7. peculiar    | 17. fire extinguisher |
| 8. skeptical   | 18. Episcopal church  |
| 9. fudgesicle  | 19. statistician      |
| 10. vulnerable | 20. Nicaragua         |

Slide 31

## Speech Phrases Task (SPT)

- |                     |                       |
|---------------------|-----------------------|
| 1. blue brush       | 13. he makes shirts   |
| 2. sea shells       | 14. bright blue beam  |
| 3. blue star        | 15. she sells shirts  |
| 4. just right       | 16. nine horse flies  |
| 5. black broom      | 17. big black bread   |
| 6. quite right      | 18. wastebaskets      |
| 7. snow slope       | 19. blue plaid pants  |
| 8. weak wrist       | 20. fine fruit flies  |
| 9. big farm house   | 21. small wrist band  |
| 10. dark blue hat   | 22. three small crabs |
| 11. small broom     | 23. quiet crabs claws |
| 12. Tom wears shoes | 24. mixed biscuits    |
|                     | 25. Swiss wrist watch |

Slide 32

## Lexical Stress Task (LST)

1. Practice Trials		2. Test Trials			
Item #	Stimulus	Item #	Stimulus	Item #	Stimulus
1	MOP	1	AIRPLANE	13	HAMmer
2	PUPpet	2	aWARD	14	guiTAR
		3	baBOON	15	LADder
		4	BASEBALL	16	maCHINE
		5	BATHTUB	17	PEAnut
		6	CHICKen	18	PUPpy
		7	COWBOY	19	racCOON
		8	DISHes	20	reMOTE
		9	FOOTBALL	21	RObot
		10	gaRAGE	22	SIDEWALK
		11	giRAFFE	23	SNOWMAN
		12	HOTDOG	24	WINdow

Slide 33

## Emphatic Stress Task (EST)

- may i see **PETE**?
- may i **SEE** pete?
- may **I** see pete?
- MAY** i see pete?
- bob may go **HOME**.
- bob may **GO** home.
- bob **MAY** go home.
- BOB** may go home.

Slide 34

## Diadochokinesis Task (DDK)

Stimulus	Number of syllables in 5 seconds (16)	Sounds were accurate	Production was rhythmic
pʌ	_____	_____	_____
kʌ	_____	_____	_____
pʌtʌ	_____	_____	_____
pʌkʌ	_____	_____	_____
tʌkʌ	_____	_____	_____
pʌtʌkʌ	_____	_____	_____
pattycake	_____	_____	_____

Slide 35

## Nonword Repetition Task (NRT)<sup>a</sup>

- |            |                   |
|------------|-------------------|
| 1. nāīb    | 9. tʃinōītāūb     |
| 2. vōūp    | 10. nāītʃōūvēīb   |
| 3. tāūɟ    | 11. dōītāūvæb     |
| 4. dōīf    | 12. tēīvōītʃāīg   |
| 5. tēīvak  | 13. vēītatʃāīdōīp |
| 6. tʃōūvæɟ | 14. dævōūnōītʃīg  |
| 7. vætʃāīp | 15. nāītʃōītāūvub |
| 8. nōītāūf | 16. tævatʃināīg   |

<sup>a</sup>Dollaghan & Campbell (1998)

Slide 36

## Syllable Repetition Task (SRT)<sup>a</sup>

- |           |              |
|-----------|--------------|
| 1. bada   | 10. dabama   |
| 2. dama   | 11. madaba   |
| 3. bama   | 12. nabada   |
| 4. mada   | 13. banada   |
| 5. naba   | 14. manaba   |
| 6. daba   | 15. bamadana |
| 7. nada   | 16. danabama |
| 8. maba   | 17. manabada |
| 9. bamana | 18. nadamaba |

<sup>a</sup>Shriberg, Lohmeier, et al. (2009)

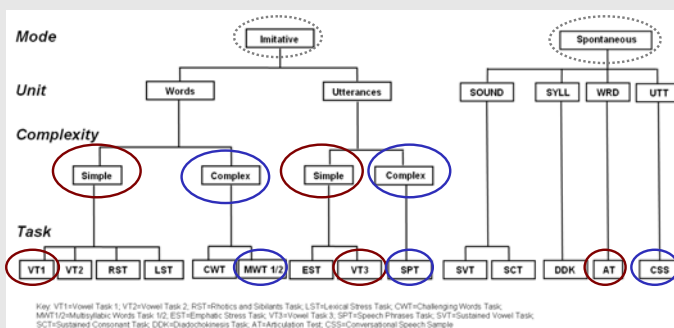
Slide 37

## Video Case Study: Performance on MSAP

- female “MN”
- 15;8 at taping
- genetic history
  - 4q-16q chromosomal translocation
  - deletion 4q terminus & duplication 16q terminus
- incoming diagnoses
  - severe CAS
  - mild-to-moderate receptive language deficits
  - severe expressive language deficits
  - mild-to-moderate MR
  - fine & gross motor deficits

Slide 38

## Video Case Study: Performance on Selected MSAP Tasks



Slide 39

## Video Samples

Slide 40

## Salient Information from MSAP Administration

Results from:

- speech sound error analyses
  - consonants & vowels
- single-word productions vs. conversational speech
- DDK tasks
- challenging & multisyllabic word tasks

Also, interesting but not differential results from:

- syllable repetition & nonword tasks

Slide 41

## Issues in Administration of MSAP

- Surprised to find a number of children who actually talked more in response to “the talking computer”
- Loss of data frustrating, secondary to children with:
  - very low speech competence
  - significant receptive language deficits
  - significant expressive language deficits
  - severe speech unintelligibility
  - attention deficits
  - cognitive deficits
  - a younger age

Slide 42

## Procedure Used by Dr. Strand to Classify Participants' Speech Status

### Procedure

- Each video or audio tape of the MSAP for each child was judged with respect to:
  - The presence or absence of 10 speech behaviors identified as being characteristic of CAS
  - The presence or absence of 10 speech behaviors identified as being characteristic of dysarthria

Slide 43

## Criteria for Identification as CAS

- Observation of at least 4 of 10 speech characteristics frequently associated with CAS
- One or more of the characteristics must be observed in at least 3 of the MSAP tasks

Slide 44

## Dr. Strand's Diagnostic Markers and Classification Criteria for CAS<sup>a</sup>

"For a judgment of the presence of CAS, the child had to exhibit vowel distortions and at least 3 of the following 10 characteristics in at least 3 of the tasks:

- difficulty achieving initial articulatory configurations or
- transitional movement gestures
- equal stress or lexical stress errors
- distorted substitutions
- syllable segregation
- groping
- intrusive schwa
- voicing errors
- slow rate
- slow DDK
- increased difficulty with multisyllabic words"

<sup>a</sup>Shriberg, L.D., Potter, N.L., & Strand, E.A. (in press)

Slide 45

## Criteria for Identification as Dysarthric

- Observation of 3/10 selected speech characteristics
- One or more of the characteristics must be observed in at least 3 of the MSAP tasks

Slide 46

## Characteristics related to Dysarthria

- Scanning speech (SS)
- Equal stress (ES)
- Sound distortions (SD)
- Irregular diadochokinetic rate (ataxia) (DDK)
- Slow rate (SR)
- Reduced range of motion (RRM)

Slide 47

## Characteristics related to Dysarthria

- Reduced strength of articulatory contacts (RS)
- Reduced respiratory support or respiratory incoordination (RRS-I)
- Strained or breathy phonatory quality (PO)
- Adventitious movement (AD)

Slide 48

## Example of Worksheet Summary

Participant ID	GAL 2 M14 O3
S/F Exam	Normal
DDK	Slow; awkward;
NRT	Poor vowel content; vowel distortions
EST	Stress errors; slow rate
VT1	Vowel distortions; groping
VT2	Separates consonants in blends; intrusive schwa; gropes
VT3	Many vowel distortions; difficulty remembering sentences
ES Comments	severe vowel distortions; slow rate, with segmentation; deliberate speech; stress errors; some consonant distortions
ES Diagnosis	CAS

Slide 49

## Methods: Madison Data Reduction

### PEPPER Environment

#### Perceptual

Narrow phonetic transcription

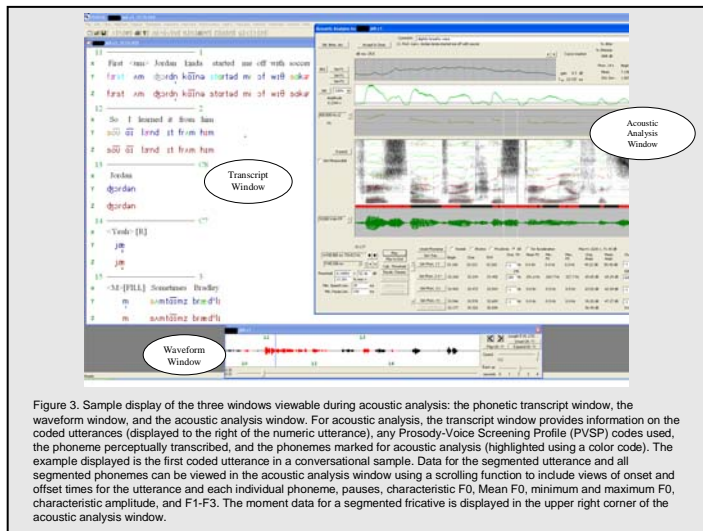
Prosody-Voice Screening Profile coding

#### Acoustic

TF32-Active X

Automated; high throughput

Slide 50



Slide 51

## Diagnostic Markers of Childhood Apraxia of Speech

- I. Rationale
  - A. Genomic
  - B. Diagnostic
- II. Methods
  - A. Data Acquisition and Reduction
  - B. Analytic Framework
  - C. Methodological Constraints
- III. Results
  - A. Promising Diagnostic Markers
  - B. Group and Subgroup Comparisons
- IV. Discussion

Slide 52

## Dr. Strand's Diagnostic Markers and Classification Criteria for CAS<sup>a</sup>

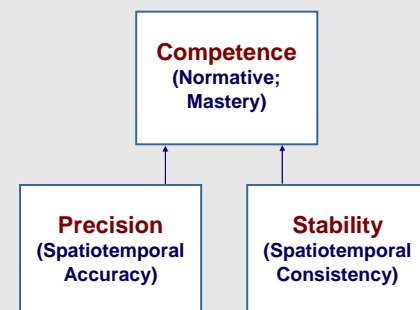
"For a judgment of the presence of CAS, the child had to exhibit vowel distortions and at least 3 of the following 10 characteristics in at least 3 of the tasks:

- difficulty achieving initial articulatory configurations or
- transitional movement gestures
- equal stress or lexical stress errors
- distorted substitutions
- syllable segregation
- groping
- intrusive schwa
- voicing errors
- slow rate
- slow DDK
- increased difficulty with multisyllabic words"

<sup>a</sup>Shriberg, L.D., Potter, N.L., & Strand, E.A. (in press)

Slide 53

## Competence, Precision, Stability Analytics (CPSA)<sup>a</sup>



<sup>a</sup>Shriberg et al. (2010)

Slide 54

## CPSA Competence Indices (30)<sup>a</sup>

Tier	Domain	Index
<b>Segmental</b>		
	<b>1. Vowels</b>	Percentage of Non-rhotic Vowels/Diphthongs Correct Percentage of Rhotic Vowels/Diphthongs Correct Percentage of Phonemic Diphthongs Correct Percentage of Vowels/Diphthongs Correct: CS Percentage of Vowels/Diphthongs Correct: AT Percentage of Non-rhotic Vowels/Diphthongs Correct Revised Percentage of Rhotic Vowels/Diphthongs Correct Revised Percentage of Phonemic Diphthongs Correct Revised Percentage of Vowels/Diphthongs Correct Revised: CS Percentage of Vowels/Diphthongs Correct Revised: AT Percentage of Relative Non-rhotic Vowel/Diphthong Distortions
	<b>2. Consonants</b>	Percentage of Consonants in Inventory Percentage of Consonants Correct: CS Percentage of Consonants Correct: AT Percentage of Consonants Correct Revised: CS Percentage of Consonants Correct Revised: AT Percentage of Consonants Correct in Complex Words: MWT Relative Omission Index Relative Substitution Index Relative Distortion Index Speech Disorders Classification System Intelligibility Index Percentage of Structurally Correct Words
	<b>3. Vowels &amp; Consonants</b>	
<b>Suprasegmental</b>		
	<b>4. Phrasing</b>	Percentage Appropriate Phrasing
	<b>5. Rate</b>	Percentage Appropriate Rate
	<b>6. Stress</b>	Percentage Appropriate Stress
	<b>7. Loudness</b>	Percentage Appropriate Loudness
	<b>8. Pitch</b>	Percentage Appropriate Pitch
	<b>9. Laryngeal Quality</b>	Percentage Appropriate Laryngeal Quality
	<b>10. Resonance Quality</b>	Percentage Appropriate Resonance Quality

<sup>a</sup> All competence indices obtained by perceptual methods (phonetic transcription; prosody-voice coding)

Slide 55

## CPSA Precision and Stability Indices (57)<sup>a</sup>

Segmental	Precision	Stability
<b>1. Vowels</b>	A Reduced Vowel Space A Lengthened Vowels A Distorted Rhotics A Reduced Pairwise Vowel Duration Variability	A Less Stable Vowel Space A Less Stable F1 A Less Stable F2 A Less Stable Vowel Duration A Less Stable Rhotic Distortions: F3-F2 A Less Stable Vowel Errors
<b>2. Consonants</b>	Nasal Emissions Reduced % Glides Correct A Lowered Sibilant Centroids A Lengthened Cluster Durations	A Less Stable Consonant Errors A Less Stable Sibilant Centroids
<b>3. Vowels and Consonants</b>	A Increased Percentage of Phoneme Distortions A Syllable/Word Segregation: Increased % Between/Within Word Pauses	A Less Stable Whole Word Errors A Less Stable % Phonemes Correct in Complex Words
<b>Suprasegmental</b>		
<b>4. Phrasing</b>	A Increased Repetitions and Revisions	A Reduced Speech-Pause Duration Variability Ratio
<b>5. Rate</b>	A Slower Speaking Rate A Slower Articulation Rate	A Less Stable Speaking Rate A Less Stable Articulation Rate
<b>6. Stress</b>	A Reduced Lexical Stress A Increased Emphatic Stress A Reduced Sentential Stress	A Less Stable Lexical Stress A Less Stable Emphatic Stress A Less Stable Sentential Stress
<b>7. Loudness</b>	A Reduced Vowels-Consonants Intensity Ratios A Increased Vowels-Consonants Intensity Ratios	A Less Stable Vowels-Consonants Intensity Ratios
<b>8. Pitch</b>	A Lowered Fundamental Frequency Mean A Raised Fundamental Frequency Mean A Lowered Fundamental Frequency Range A Increased Fundamental Frequency Range	A Less Stable Mean Fundamental Frequency
<b>9. Laryngeal Quality</b>	A Increased Jitter A Increased Shimmer A Reduced Harmonics-to-Noise Ratio A Increased % Breathily Utterances A Increased % Rough Utterances A Increased % Strained Utterances A Increased % Break/Shift/Tremorous Utterances	A Less Stable Jitter A Less Stable Shimmer A Less Stable Harmonics-to-Noise Ratio
<b>10. Resonance Quality</b>	A Increased % Nasal Utterances A Nasal: Lowered F1: /o/ A Increased % of Nasopharyngeal Utterances A Nasopharyngeal: Lowered F2: High Vowels	A Less Stable Nasal: Lowered F1: /o/ A Nasopharyngeal: Less Stable F2: High Vowels

<sup>a</sup>Acoustic Analyses

Slide 56

## 25 Putative CPSA Markers of MSD-AOS

Segmental	Precision	Stability
<b>1. Vowels/Diphthongs</b>		A Less Stable Vowel Space A Less Stable F1 A Less Stable F2 A Less Stable Vowel Duration A Less Stable Rhotic Distortions: F3-F2 A Less Stable Vowel Errors
<b>2. Consonants</b>	Reduced % Glides Correct	A Less Stable Consonant Errors A Less Stable Sibilant Centroids
<b>3. Vowels/Diph &amp; Consonants</b>		A Less Stable Whole Word Errors A Less Stable % Phonemes Correct in Complex Words
<b>Suprasegmental</b>		
<b>4. Phrasing</b>	A Increased Repetitions and Revisions	A Reduced Speech-Pause Duration Variability Ratio
<b>5. Rate</b>		A Less Stable Speaking Rate A Less Stable Articulation Rate
<b>6. Stress</b>		A Less Stable Lexical Stress A Less Stable Emphatic Stress A Less Stable Sentential Stress
<b>7. Loudness</b>		A Less Stable Vowels-Consonants Intensity Ratios
<b>8. Pitch</b>		A Less Stable Mean Fundamental Frequency
<b>9. Laryngeal Quality</b>		A Less Stable Jitter A Less Stable Shimmer A Less Stable Harmonics-to-Noise Ratio
<b>10. Resonance Quality</b>		A Less Stable Nasal: Lowered F1: /o/ A Nasopharyngeal: Less Stable F2: High Vowels

Slide 57

## 12 Putative CPSA Markers of MSD-DYS

Segmental	Precision	Stability
<b>1. Vowels/Diphthongs</b>		
<b>2. Consonants</b>	Nasal Emissions	
<b>3. Vowels/Diph &amp; Consonants</b>		
<b>Suprasegmental</b>		
<b>4. Phrasing</b>		
<b>5. Rate</b>		
<b>6. Stress</b>		
<b>7. Loudness</b>		
<b>8. Pitch</b>	A Lowered Fundamental Frequency Mean A Lowered Fundamental Frequency Range	
<b>9. Laryngeal Quality</b>	A Increased Jitter A Increased Shimmer A Reduced Harmonics-to-Noise Ratio A Increased % Breathily Utterances A Increased % Rough Utterances A Increased % Strained Utterances A Increased % Break/Shift/Tremorous Utterances	
<b>10. Resonance Quality</b>	A Increased % Nasal Utterances A Nasal: Lowered F1: /o/	

Slide 58

## 20 Putative CPSA Markers of MSD-NOS

Segmental	Precision	Stability
<b>1. Vowels/Diphthongs</b>	A Reduced Vowel Space A Lengthened Vowels A Distorted Rhotics A Reduced Pairwise Vowel Duration Variability	
<b>2. Consonants</b>	A Lowered Sibilant Centroids A Lengthened Cluster Durations	
<b>3. Vowels/Diph &amp; Consonants</b>	A Increased Percentage of Phoneme Distortions A Syllable/Word Segregation: Increased % Between/Within Word Pauses	
<b>Suprasegmental</b>		
<b>4. Phrasing</b>		
<b>5. Rate</b>	A Slower Speaking Rate A Slower Articulation Rate	
<b>6. Stress</b>	A Reduced Lexical Stress A Increased Lexical Stress A Reduced Emphatic Stress A Reduced Sentential Stress	
<b>7. Loudness</b>	A Reduced Vowels-Consonants Intensity Ratios A Increased Vowels-Consonants Intensity Ratios	
<b>8. Pitch</b>	A Raised Fundamental Frequency Mean A Increased Fundamental Frequency Range	
<b>9. Laryngeal Quality</b>		
<b>10. Resonance Quality</b>	A Increased % of Nasopharyngeal Utterances A Nasopharyngeal: Lowered F2: High Vowels	

Slide 59

## Procedure To Classify Participants as “Positive” on Each Candidate Index

### Biobehavioral indices

- For indices that do not quantify speech-sound errors (e.g., Vowel Space, Vowel Duration, F2 Formant Stability), Z-scores were derived from the **Typical Speaker database**.
- Z-scores beyond 1 SD (i.e., less precise, less stable) were classified as ‘positive’ for that candidate diagnostic marker of motor speech disorder.

### Speech error indices

- For 8 indices that quantify speech-sound errors (e.g., Percentage of Non-Rhotic Vowels Correct; Percentage of Glides Correct), Z-scores were derived from the **Speech Delay database**.
- Z-scores beyond 1 SD (i.e., less precise, less stable) were classified as ‘positive’ for that candidate marker of motor speech disorder.

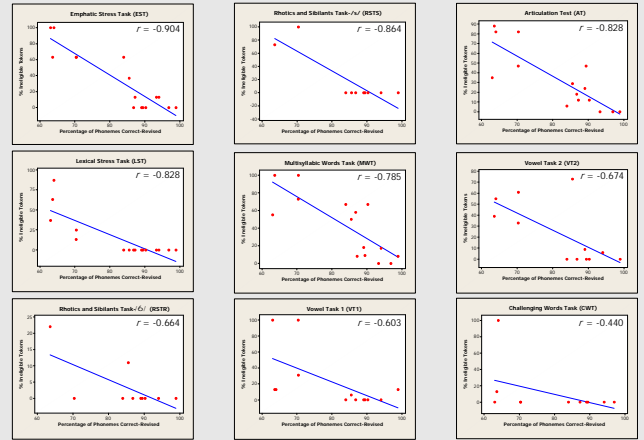
Slide 60

# Diagnostic Markers of Childhood Apraxia of Speech

- I. Rationale
  - A. Genomic
  - B. Diagnostic
- II. **Methods**
  - A. Data Acquisition and Reduction
  - B. Analytic Framework
  - C. **Methodological Constraints**
- III. Results
  - A. Promising Diagnostic Markers
  - B. Group and Subgroup Comparisons
- IV. Discussion

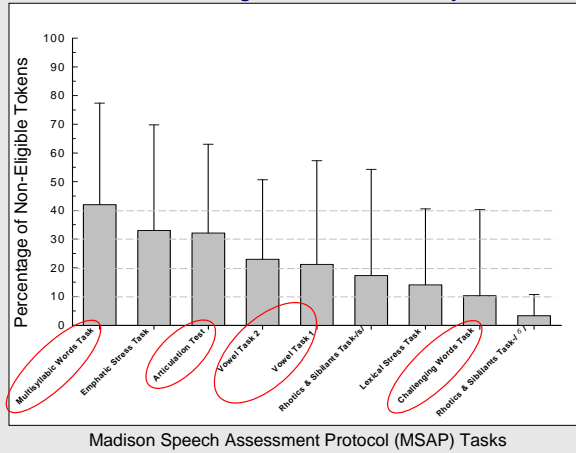
Slide 61

# Methodological Constraints: Percentage of Ineligible Tokens for Acoustic Analyses on MSAP Tasks is Negatively Associated with Percentage of Phonemes Correct-Revised



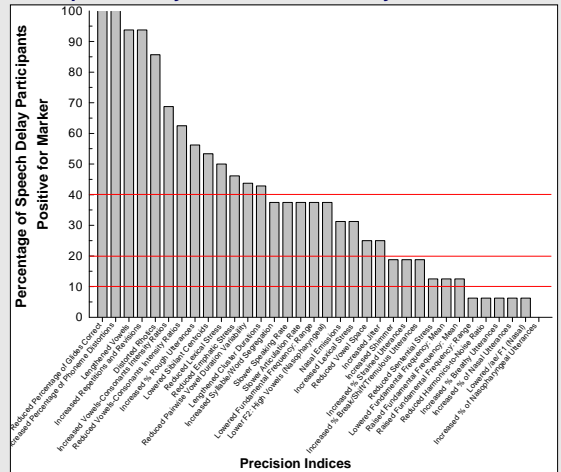
Slide 62

# Methodological Constraints: Participants with CAS have a High Percentage of Tokens that are Not Eligible for Acoustic Analyses



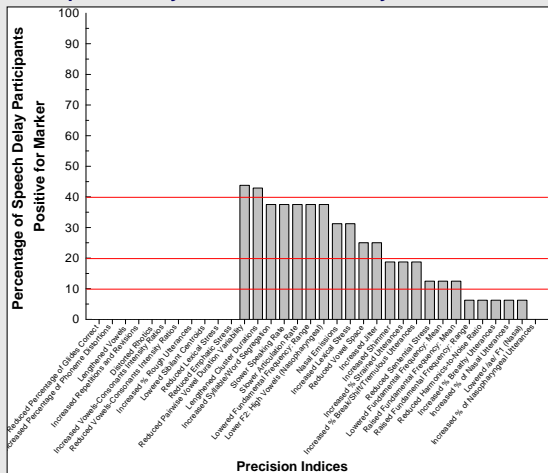
Slide 63

# Methodological Constraints: Children with Speech Delay are 'Positive' on Many Putative Markers of CAS



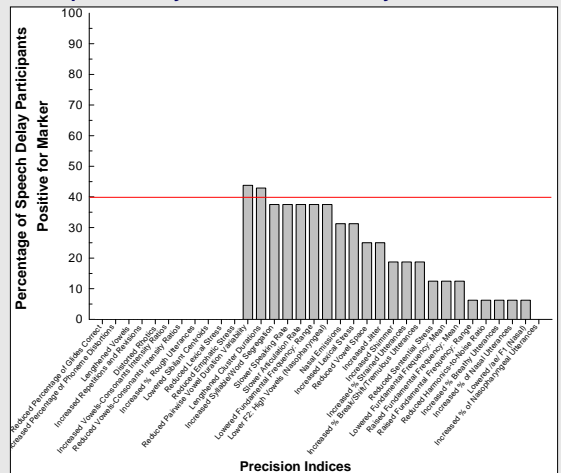
Slide 64

# Methodological Constraints: Children with Speech Delay are 'Positive' on Many Putative Markers of CAS

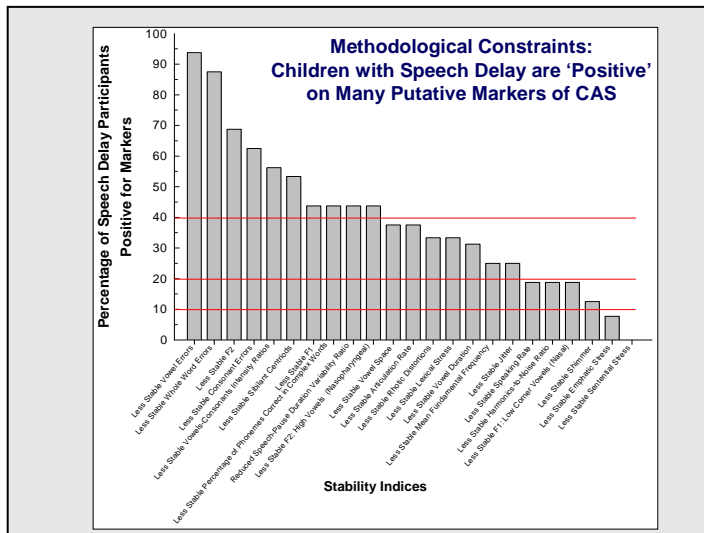


Slide 65

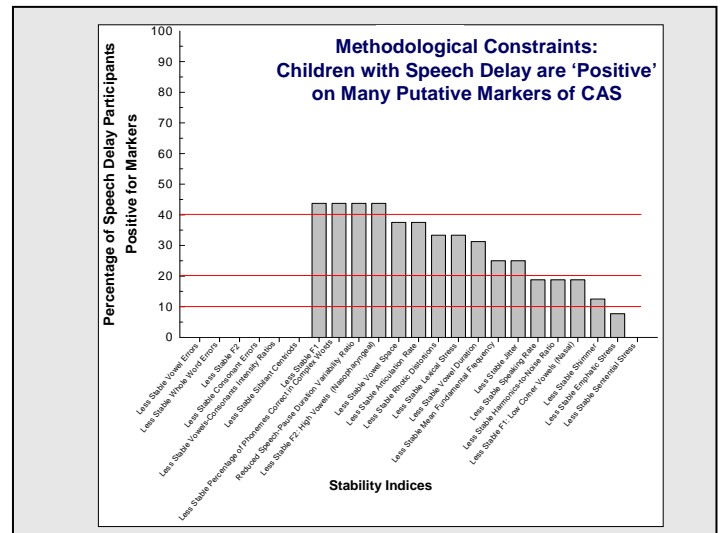
# Methodological Constraints: Children with Speech Delay are 'Positive' on Many Putative Markers of CAS



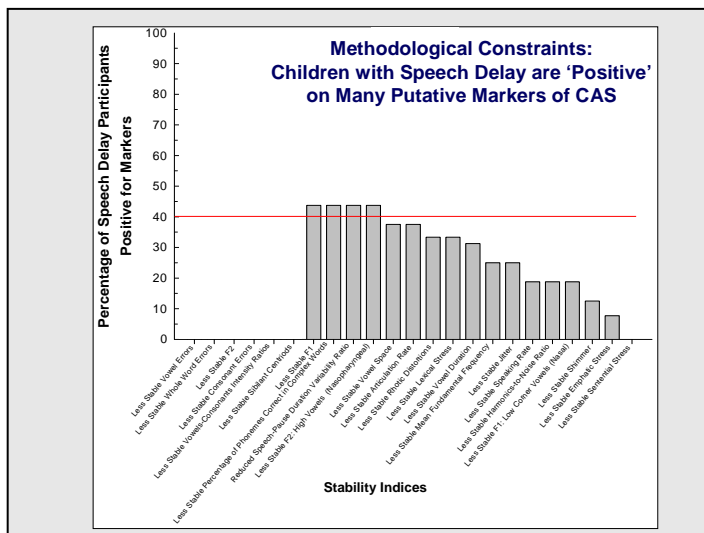
Slide 66



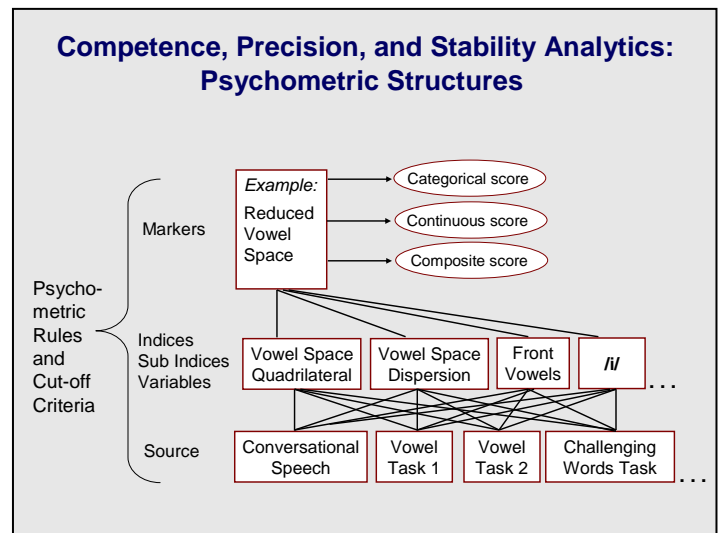
Slide 67



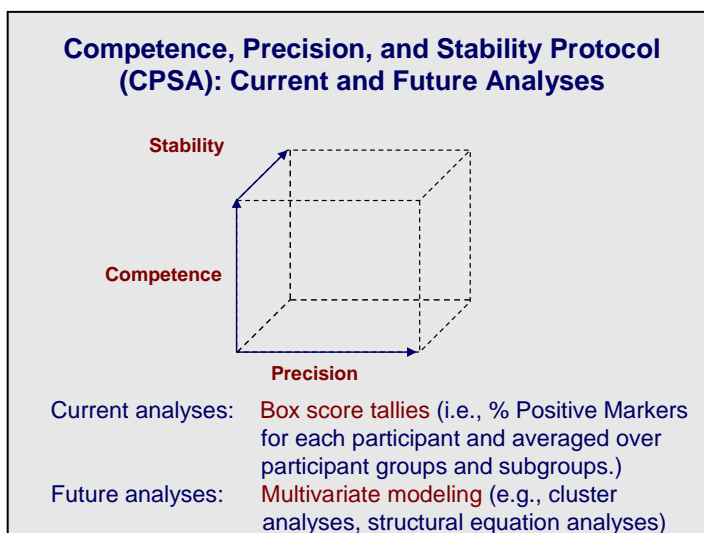
Slide 68



Slide 69



Slide 70



Slide 71

- Diagnostic Markers of Childhood Apraxia of Speech**
- I. Rationale
    - A. Genomic
    - B. Diagnostic
  - II. Methods
    - A. Data Acquisition and Reduction
    - B. Analytic Framework
    - C. Methodological Constraints
  - III. Results
    - A. Promising Diagnostic Markers
    - B. Group and Subgroup Comparisons
  - IV. Discussion

Slide 72

## 'Top 7' Potential Diagnostic Markers of CAS for 16 Participants with Idiopathic CAS

Domain	Index*	Diagnostic Accuracy					
		Analytic		Effect Size*	90% Confidence Interval	Sensitivity	Specificity
		Precision	Stability				
Vowels	Less Stable F1		X	1.173*	0.943, 2.031	93.3	56.3
	Less Stable Vowel Duration		X	1.208*	1.010, 2.163	86.7	68.8
Vowels & Consonants	Less Stable % Phonemes Correct In Complex Words		X	0.769*	0.475, 1.184	80.0	56.3
Rate	Slower Speaking Rate	X		1.144*	0.795, 2.091	88.9	62.5
	Slower Articulation Rate	X		1.144*	0.795, 2.091	88.9	62.5
Pitch	Raised Fundamental Frequency Mean	X		1.334*	1.145, 2.251	73.3	87.5
Resonance Quality	Lower F2: High Vowels (Nasopharyngeal)	X		0.896*	0.668, 1.939	80.0	62.5

\* Bold entries indicate candidate marker analysis completed using acoustic data reduction methods.  
 † Significant Cohen arcsine transformation effect size for two 1-sided tests of proportional differences (StaXact-5, 2001; Brown, 2009).

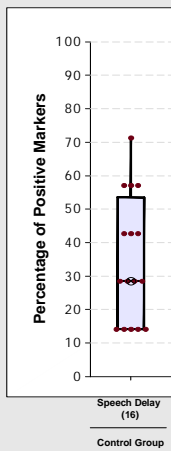
Slide 73

## Diagnostic Markers of Childhood Apraxia of Speech

- I. Rationale
  - A. Genomic
  - B. Diagnostic
- II. Methods
  - A. Data Acquisition and Reduction
  - B. Analytic Framework
  - C. Methodological Constraints
- III. Results
  - A. Promising Diagnostic Markers
  - B. Group and Subgroup Comparisons
- IV. Discussion

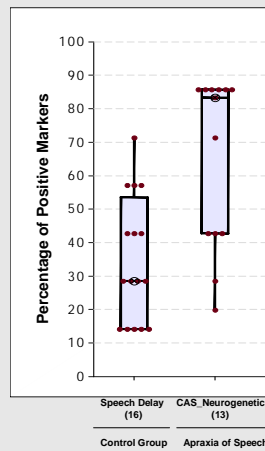
Slide 74

### Percentage of Positive Markers ('Top 7 Indices') for Participants in the Study Groups and Subgroups



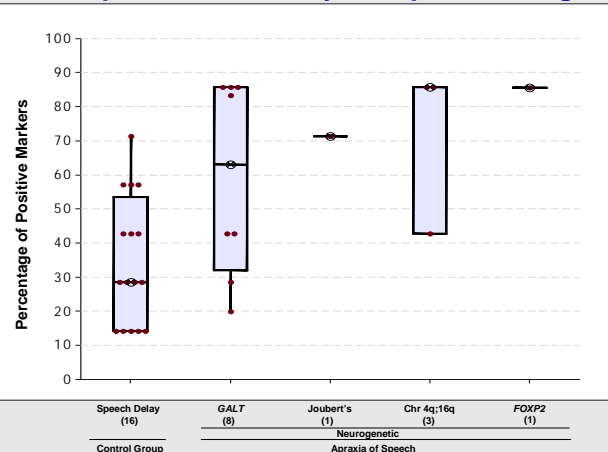
Slide 75

### Percentage of Positive Markers ('Top 7 Indices') for Participants in the Study Groups and Subgroups



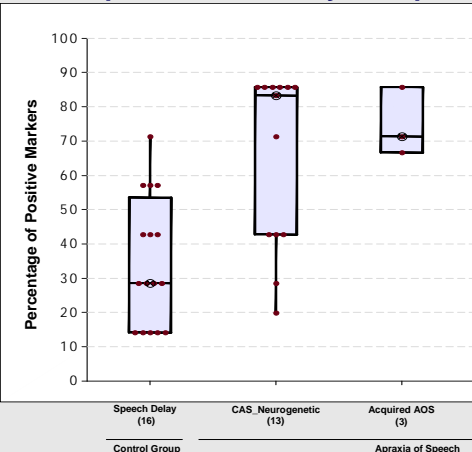
Slide 76

### Percentage of Positive Markers ('Top 7 Indices') for Participants in the Study Groups and Subgroups



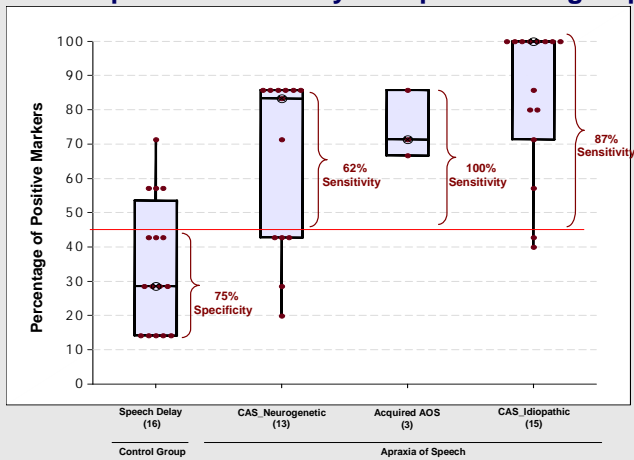
Slide 77

### Percentage of Positive Markers ('Top 7 Indices') for Participants in the Study Groups and Subgroups



Slide 78

## Percentage of Positive Markers ('Top 7 Indices') for Participants in the Study Groups and Subgroups



Slide 79

## Conclusions and Research Questions

### Four Premises Underlying CAS Diagnostic Markers Research

- ❑ Phenotype Constraints remain the major need in Genomic, Diagnostic, and Other CAS Research
- ❑ Identifying Markers of CAS in Neurologic and Neurodevelopment Contexts will inform markers of Idiopathic CAS
- ❑ Validated Behavioral Markers of CAS will inform explanatory accounts of CAS
- ❑ A Conventional, Three-Phase Speech Processing Perspective provides a sufficient framework for an explanatory account of CAS

Slide 80

## Conclusions

1. Methodological constraints and heterogeneities in phenotype expression require a considerably larger database of participants (including participants with subtypes of dysarthria) before the major questions of this research can be addressed using multivariate statistics.

Slide 81

## Conclusions

1. Methodological constraints and heterogeneities in phenotype expression require a considerably larger database of participants (including participants with subtypes of dysarthria) before the major questions of this research can be addressed using multivariate statistics.
2. Findings to date from the present and other small data sets support the premises that an operationalized and standardized set of perceptual and acoustic markers of Idiopathic CAS can be identified from a research framework that includes children and adult participants with apraxia of speech in complex neurodevelopmental and neurologic contexts.

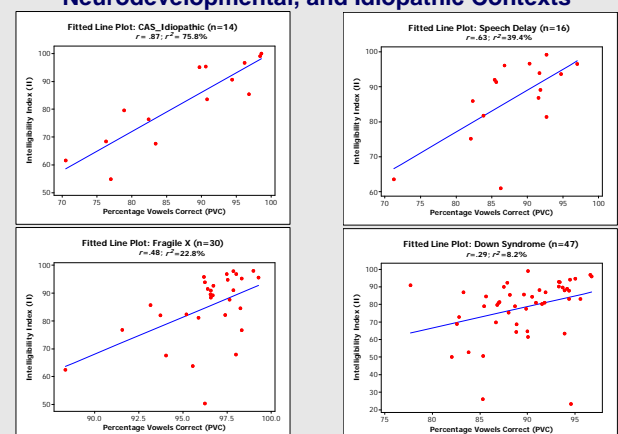
Slide 82

## Conclusions

3. Findings to date from the present and other studies indicate that the core diagnostic markers of CAS will likely:
  - ❑ index variables within the linguistic domains of Vowels, Phrasing, Rate, Stress, and Resonance
  - ❑ include both spatial and temporal indices and quantify both precision and stability
  - ❑ be identified within assessment tasks that accommodate individual differences in biological age, cognitive-linguistic status, and minimal speech competence
  - ❑ require researchers/clinicians to have data reduction skills in perceptual and acoustic analyses systems
    - possibility of short-forms and speech recognition technology

Slide 83

## Current Research Focus: Vowel Productions in Participants with CAS in Neurologic, Neurodevelopmental, and Idiopathic Contexts



Slide 84

## Research Questions

1. Why do so many children, adolescents, and adults **classified as having apraxia of speech** have a **low Percentage of Positive Markers for apraxia of speech** (i.e., impacting the **sensitivity** of potential markers of apraxia of speech)?

Possible explanations:

- They are **true negatives for MSD**.

The classification criteria used to classify CAS/AOS by the third author yields some **invalid classifications**. Classic categorical distinctions among subtypes of MSD may need to be re-evaluated. Developmental differences in severity of expression may be a primary moderating variable in classification.

Slide 85

## Research Questions

- They are **true positives for MSD**, but **MSAP and CPSA methods are not sufficiently sensitive for MSD-AOS**.

The low Percentage of Positive Markers for MSD-AOS is **due to assessment/data reduction sensitivity issues** (i.e., core signs of their CAS are **not identified** by the current MSAP and CPSA analytics; **excessive data loss** on core signs of CAS due to low speech competence).

- **Other explanations?**

Slide 86

## Research Questions

2. Why do so many children with Speech Delay (SD) have a high Percentage of Positive Markers for MSD (i.e., impacting the **specificity** of potential markers of CAS)?

Possible explanations:

- They are **false positives for any subtype of MSD**.

The high Percentage of Positive Markers for MSD is due to **methodological issues** (e.g., criteria for 'positive' z-score [ $>1$  standard deviation] is **too liberal**; positive scores come from **different MSAP tasks** than those in true MSD; **other**).

Slide 87

## Research Questions

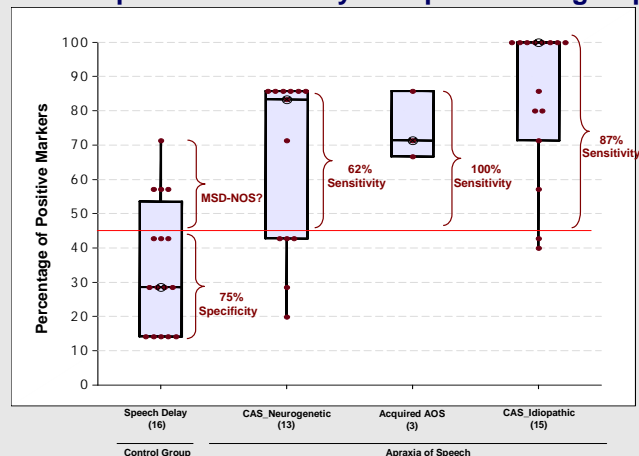
- They are **true positives for MSD-NOS**.

They have **some form of a delay or difference in speech motor development** that does not meet criteria for apraxia (MSD-AOS) or any subtype of dysarthria (MSD-DYS).

- **Other explanations?**

Slide 88

## Percentage of Positive Markers ('Top 7 Indices') for Participants in the Study Groups and Subgroups



Slide 89

## Research Directions

- **Increase database of participants** with CAS in neurologic, complex neurodevelopmental, and idiopathic contexts, including participants with subtypes of dysarthria
- Develop speech tasks that **maximize obtained speech tokens eligible for acoustic analyses**
- Complete psychometric studies to determine **optimum cut-off points for 'positive' status** on potential markers of CAS
- Complete task-dependent analyses to determine **which MSAP tasks and subscales are optimally sensitive and specific** for each potential marker of CAS

Slide 90

## Research Directions

- ❑ Complete acoustic analyses of Vowels, Phrasing, Rate, Stress, and Resonance data toward explanatory accounts of CAS associated with core deficits in planning/programming
- ❑ Forthcoming collaborative studies of the hypothesis of apraxia of speech in other complex neurodevelopmental disorders:
  - Autism (Shriberg, Paul, Black, & van Santen, in press)
  - Down syndrome (Wilson; Abbeduto; Camarata)
  - Fragile X syndrome (Abbeduto)
  - Galactosemia (Potter, Strand)
  - Velocardiofacial syndrome (Baylis)

Slide 91

## References

- Bishop, D. V. M. (2009). Genes, cognition, and communication. *Annals of the New York Academy of Sciences*, 1156, 1-18.
- Brown, R. L. (2009). *ESCalc: Software for calculation of exact proportional difference effect size confidence intervals version 1.00*. Madison, WI: Research Design & Statistics Unit, University of Wisconsin-Madison, March 2009.
- Brunetti-Pierri, N., Paciorkowski, A. R., Ciccone, R., Della Mina, E., Bonaglia, M. C., Borgatti, R., et al. (in press). Duplications of FOXP1 in 14q12 are associated with developmental epilepsy, mental retardation, and severe speech impairment. *European Journal of Human Genetics*.
- Carr, C. W., Moreno-De-Luca, D., Parker, C., Zimmerman, H. H., Ledbetter, N., Martin, C. L., et al. (2010). Chiari I malformation, delayed gross motor skills, severe speech delay, and epileptiform discharges in a child with FOXP1 haploinsufficiency. *European Journal of Human Genetics*, 18, 1216-1220.
- Dollaghan, C., & Campbell, T. F. (1998). Nonword repetition and child language impairment. *Journal of Speech, Language, and Hearing Research*, 41, 1136-1146.
- Grigorenko, E. L. (2009). Speaking genes or genes for speaking? Deciphering the genetics of speech and language. *The Journal of Child Psychology and Psychiatry*, 50, 116-125.
- Hamdan, F. F., Daoud, H., Rochefort, D., Piton, A., Gauthier, J., Langlois, M., et al. (in press). De novo mutations in FOXP1 in cases with intellectual disability, autism, and language impairment. *The American Journal of Human Genetics*.
- Hom, D., Kapeller, J., Rivera-Brugués, N., Moog, U., Lorenz-Depiereux, B., Eck, S., et al. (in press). Identification of FOXP1 deletions in three unrelated patients with mental retardation and significant speech and language deficits. *Human Mutation*.

Slide 92

## References

- Kogan, J. M., Miller, E., & Ware, S. M. (2009). High resolution SNP based microarray mapping of mosaic supernumerary marker chromosomes 13 and 17: Delineating novel loci for apraxia. *American Journal of Medical Genetics Part A*, 149A: 887-893.
- Lewis, B. (October, 2010). *Genetic and neurological correlates of childhood apraxia of speech*. Paper presented for the Childhood Apraxia of Speech Virtual Conference, University of Wisconsin-Eau Claire, Eau Claire, WI.
- Maassen (2002). Issues contrasting adult acquired versus developmental apraxia of speech. *Seminars in Speech and Language*, 23, 257-266.
- McNeil, M. R. (2001). The assiduous challenge of defining and explaining apraxia of speech. In B. Maassen, W. Hulstijn, R. D. Kent, H. F. M. Peters, & P. H. H. M. van Lieshout (Eds.), *Speech Motor Control in Normal and Disordered Speech: Proceedings of the 4th International Speech Motor Conference* (pp. 337-342) Nijmegen: Uitgeverij Vantilt.
- Newbury, D. F. & Monaco, A. P. (2010). Genetic advances in the study of speech and language disorders. *Neuron*, 68, 309-320.
- Pal, D. K., Li, W., Clarke, T., Lieberman, P., & Strug, L. J. (in press). Pleiotropic effects of the 11p13 locus on developmental dyspraxia and EEG centrottemporal sharp waves. *Genes, Brain, and Behavior*.
- Pariani, M. J., Spencer, A., Graham, J. M., & Rimoin, D. L. (2009). A 785 kb deletion of 3p14.1p13, including the FOXP1 gene, associated with speech delay, contractures, hypertononia and blepharophimosis. *European Journal of Medical Genetics*, 52, 123-127.
- Ramus, F. & Fisher, S. E. (2009). Genetics of language. In M. S. Gazzaniga (Ed.), *The Cognitive Neurosciences IV* (pp. 855-872). Cambridge, MA: MIT Press.

Slide 93

## References

- Roll, P., Vernes, S. C., Bruneau, N., Cillario, J., Ponsolle-Lenfant, M., Massacrier, A., et al. (in press). Molecular networks implicated in speech-related disorders: FOXP2 regulates the SRPX2/uPAR complex. *Human Molecular Genetics*.
- Shriberg, L. D. (2010). A neurodevelopmental framework for research in Childhood Apraxia of Speech. In B. Maassen & P. van Lieshout (Eds.), *Speech Motor Control: New developments in basic and applied research* (pp. 259-270). Oxford: Oxford University Press.
- Shriberg, L. D., Fourakis, M., Hall, S., Karlsson, H. K., Lohmeier, H. L., McSweeney, J., Potter, N. L., Scheer Cohen, A. R., Strand, E. A., Tilkens, C. M., & Wilson, D. L. (2010). Extensions to the Speech Disorders Classification System (SDCS). *Clinical Linguistics & Phonetics*, 24, 795-824.
- Shriberg, L. D., Lohmeier, H. L., Campbell, T. F., Dollaghan, C. A., Green, J. R., & Moore, C. A. (2009). A nonword repetition task for speakers with misarticulations: The Syllable Repetition Task (SRT). *Journal of Speech, Language, and Hearing Research*, 52, 1189-1212.
- Shriberg, L. D., Paul, R., Black, L. M., & van Santen, J. P. (in press). The hypothesis of apraxia of speech in children with Autism Spectrum Disorder. *Journal of Autism and Developmental Disorders*.
- Shriberg, L. D., Potter, N. L., & Strand, E. A. (in press). Prevalence and phenotype of childhood apraxia of speech in youth with galactosemia. *Journal Speech, Language, and Hearing Research*.
- StatXact-5 for Windows (2001). *Software for Exact Nonparametric Inference*. Cytel Software Corporation, Cambridge, MA.
- Zhao, Y., Ma, H., Wang, Y., Gao, H., Xi, C., Hua, T., et al. (2010). Association between FOXP2 gene and speech sound disorder in Chinese population. *Psychiatry and Clinical Neurosciences*, 64, 565-573.

Slide 94

## Diagnostic Markers of Childhood Apraxia of Speech

- I. Rationale
  - A. Genomic
  - B. Diagnostic
- II. Methods
  - A. Data Acquisition and Reduction
  - B. Analytic Framework
  - C. Methodological Constraints
- III. Results
  - A. Promising Diagnostic Markers
  - B. Group and Subgroup Comparisons
- IV. Discussion

Slide 95

Thanks . . .



<http://www.waisman.wisc.edu/phonology/>

Slide 96