Diagnostic Markers of Childhood Apraxia of Speech

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Slide 1

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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

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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

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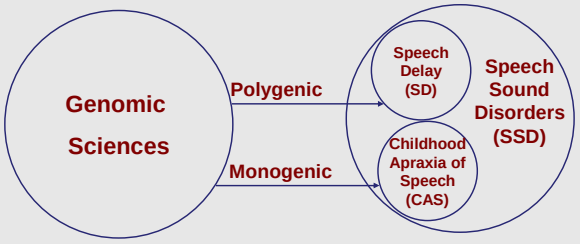
Genomic Premise 2: The Genomic Origins of CAS Can Be Identified Using Current Sequencing and Bioinformatics Methods



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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)
- *FOXG1*
  - 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)

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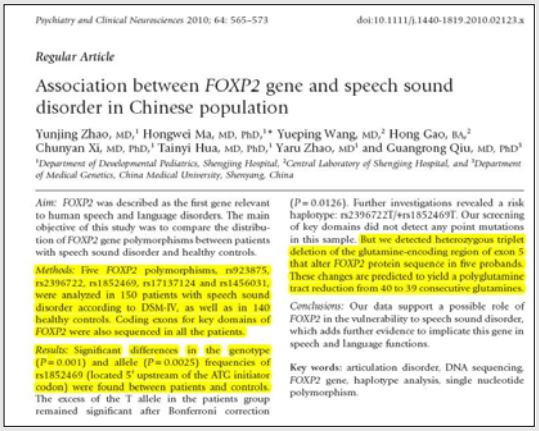
Example of Phenotype Issues: Speech Sound Disorder? Severe Speech Delay? CAS?



Psychiatry and Clinical Neurosciences 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,[1] Hongwei Ma, MD, PhD,[1]* Yueping Wang, MD,[2] Hong Gao, BA,[2] Chunyan Xi, MD, PhD,[1] Tainyi Hua, MD, PhD,[1] Yaru Zhao, MD[1] and Guangrong Qiu, MD, PhD[3]

[1]*Department of Developmental Pediatrics, Shengjing Hospital,* [2]*Central Laboratory of Shengjing Hospital, and* [3]*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, rs923875, 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 initiator 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 5 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.

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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

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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)

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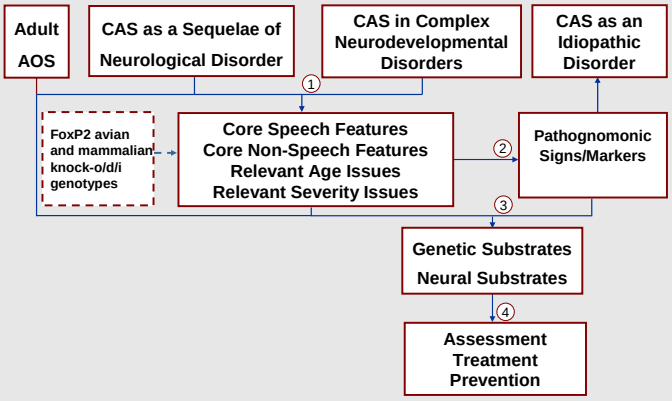
Diagnostic Premise 2: Identifying Markers of CAS in Neurologic and Neurodevelopment Contexts Will Inform Markers of Idiopathic CAS



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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?

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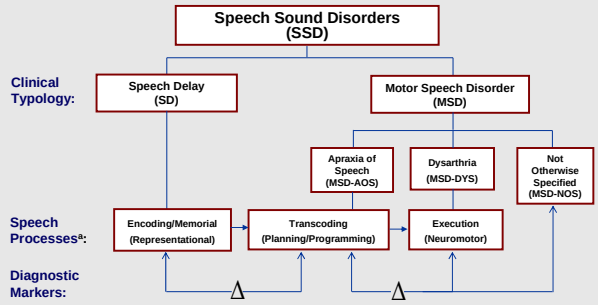
Diagnostic Premise 4:
A Conventional Three-Phase Speech Processing Perspective Provides a Sufficient Framework Toward an Explanatory Account of CAS



[a] Sources: van der Merwe; Guenther; Levelt; others

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Methods:
Five Participant Groups and Subgroups

Group				Percentage of Consonants Correct (PCC)	
Description	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	
		3	18, 23, 50	88.3	2.4
Galactosemia		8	5 - 16	67.6	20.0
Joubert Syndrome		1	11	70.0	

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Acquired Apraxia of Speech	AOS	3	45, 53, 67	92.4	4.5

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Speech Delay	SD	16	3 - 6	64.3	13.4
Typically Speaking	TS	100	3 - 16	95.7	6.1

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Methods:
Madison Speech Assessment Protocol (MSAP)[a]

- **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

[a]Shriberg et al. (2010)

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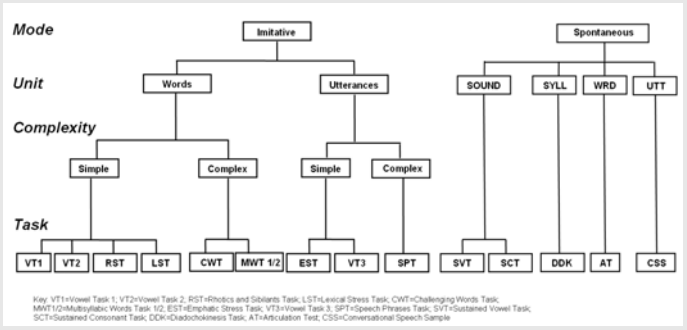
MSAP Task Hierarchy



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Sustained Vowel Task (SVT)

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

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Sustained Consonant Task (SCT)

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

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Vowel Task 1 (VT1)
Corner Vowels

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

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Vowel Task 2 (VT2)
Other Vowels & Diphthongs

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

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Vowel Task 3 (VT3)

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

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Rhotics and Sibilants Task

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

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Challenging Words Task (CWT)

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

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Multisyllabic Words Task 1 (MWT1)

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

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Multisyllabic Words Task 2 (MWT2)

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

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Speech Phrases Task (SPT)

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

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Lexical Stress Task (LST)

1. Practice Trials

Item #	Stimulus
1	MOP
2	PUPpet

2. Test Trials

Item #	Stimulus	Item #	Stimulus
1	AIRPLANE	13	HAMmer
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

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Emphatic Stress Task (EST)

1. may i see **PETE**?
2. may i **SEE** pete?
3. may **I** see pete?
4. **MAY** i see pete?
5. bob may go **HOME**.
6. bob may **GO** home.
7. bob **MAY** go home.
8. **BOB** may go home.

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Diadochokinesis Task (DDK)

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

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Nonword Repetition Task (NRT)[a]

1. naɪb
2. voʊp
3. taʊdʒ
4. dɔɪf
5. teɪvak
6. tʃoʊvæg
7. vætʃaɪp
8. nɔɪtaʊf
9. tʃinɔɪtaʊb
10. naɪtʃoʊveɪb
11. dɔɪtaʊvæb
12. teɪvɔɪtʃaɪg
13. veɪtatʃaɪdɔɪp
14. dævoʊnɔɪtʃig
15. naɪtʃɔɪtaʊvub
16. tævatʃinaɪg

[a]Dollaghan & Campbell (1998)

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Syllable Repetition Task (SRT)[a]

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

[a]Shriberg, Lohmeier, et al. (2009)

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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

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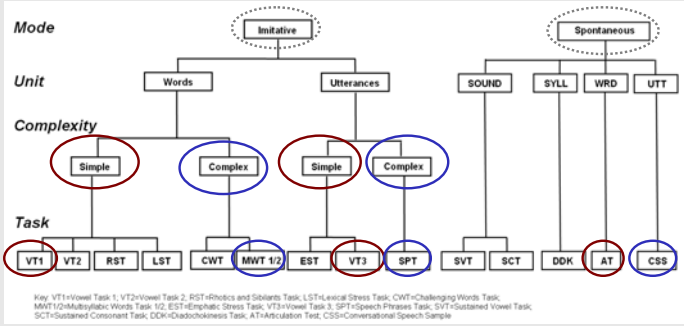
Video Case Study: Performance on Selected MSAP Tasks



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Video Samples

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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

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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

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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

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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

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Dr. Strand's Diagnostic Markers and Classification Criteria for CAS[a]

"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 transitionary 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"

[a]Shriberg, L.D., Potter, N.L., & Strand, E.A. (in press)

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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

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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)

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Characteristics related to Dysarthria

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

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Example of Worksheet Summary

Participant ID	GAL 2 M14 03
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

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Methods: Madison Data Reduction

PEPPER Environment

- Perceptual
  - Narrow phonetic transcription
  - Prosody-Voice Screening Profile coding
- Acoustic
  - TF32-Active X
  - Automated; high throughput

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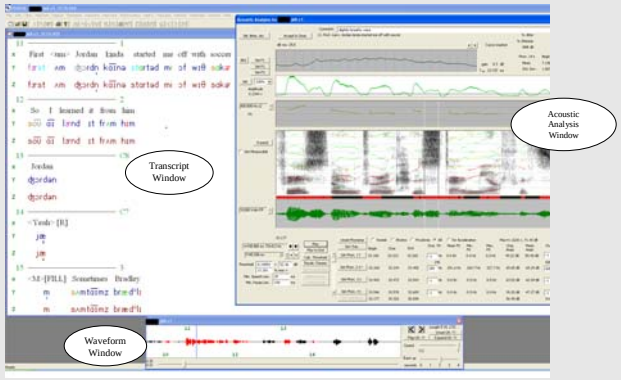

Figure 3. Sample display of the three windows viewable during acoustic analysis: the phonetic transcript window, the waveform window, and the acoustic analysis window. For acoustic analysis, the transcript window provides information on the coded utterances (displayed to the right of the numeric utterance), any Prosody-Voice Screening Profile (PVSP) codes used, the phoneme perceptually transcribed, and the phonemes marked for acoustic analysis (highlighted using a color code). The example displayed is the first coded utterance in a conversational sample. Data for the segmented utterance and all segmented phonemes can be viewed in the acoustic analysis window using a scrolling function to include views of onset and offset times for the utterance and each individual phoneme, pauses, characteristic F0, Mean F0, minimum and maximum F0, characteristic amplitude, and F1-F3. The moment data for a segmented fricative is displayed in the upper right corner of the acoustic analysis window.

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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

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Dr. Strand's Diagnostic Markers and Classification Criteria for CAS[a]

"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 transitionary 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"

[a]Shriberg, L.D., Potter, N.L., & Strand, E.A. (in press)

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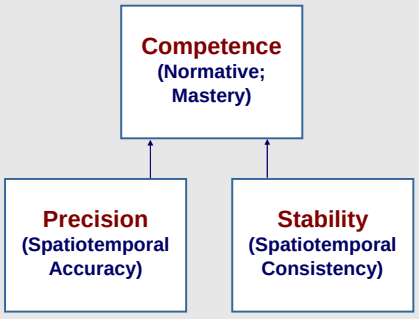
Competence, Precision, Stability Analytics (CPSA)[a]



[a]Shriberg et al. (2010)

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CPSA Competence Indices (30)[a]

Tier	Domain	Index
Segmental		
	1. Vowels	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
	2. Consonants	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
	3. Vowels & Consonants	Speech Disorders Classification System Intelligibility Index Percentage of Structurally Correct Words
Suprasegmental		
	4. Phrasing	Percentage Appropriate Phrasing
	5. Rate	Percentage Appropriate Rate
	6. Stress	Percentage Appropriate Stress
	7. Loudness	Percentage Appropriate Loudness
	8. Pitch	Percentage Appropriate Pitch
	9. Laryngeal Quality	Percentage Appropriate Laryngeal Quality
	10. Resonance Quality	Percentage Appropriate Resonance Quality

[a] All competence indices obtained by perceptual methods (phonetic transcription; prosody-voice coding)

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CPSA Precision and Stability Indices (57)[a]

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

[a]A=Acoustic Analyses

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25 Putative CPSA Markers of MSD-AOS

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

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12 Putative CSPA Markers of MSD-DYS

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

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20 Putative CPSA Markers of MSD-NOS

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

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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.

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Diagnostic Markers of Childhood Apraxia of Speech

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IV. Discussion

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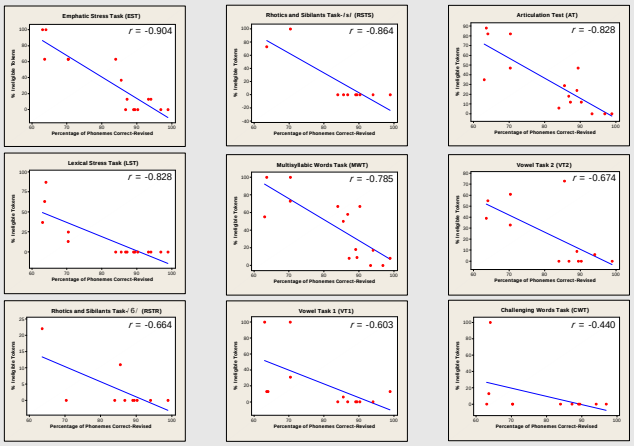
Methodological Constraints: Percentage of Ineligible Tokens for Acoustic Analyses on MSAP Tasks is Negatively Associated with Percentage of Phonemes Correct-Revised



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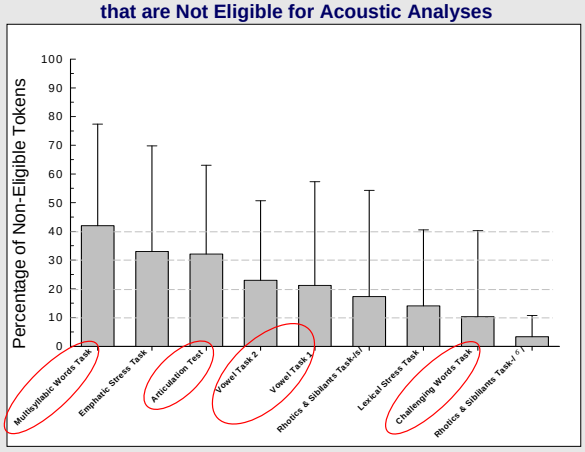
Methodological Constraints: Participants with CAS have a High Percentage of Tokens that are Not Eligible for Acoustic Analyses



Madison Speech Assessment Protocol (MSAP) Tasks

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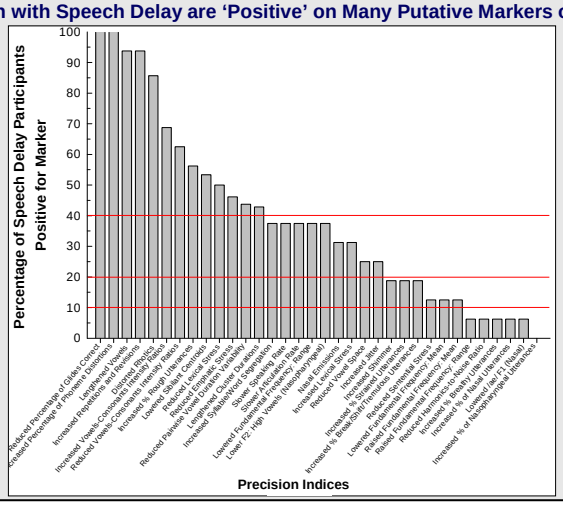
Methodological Constraints: Children with Speech Delay are 'Positive' on Many Putative Markers of CAS



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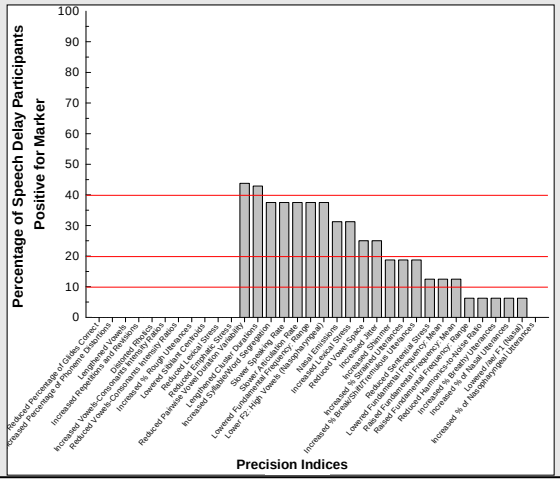
Methodological Constraints: Children with Speech Delay are 'Positive' on Many Putative Markers of CAS



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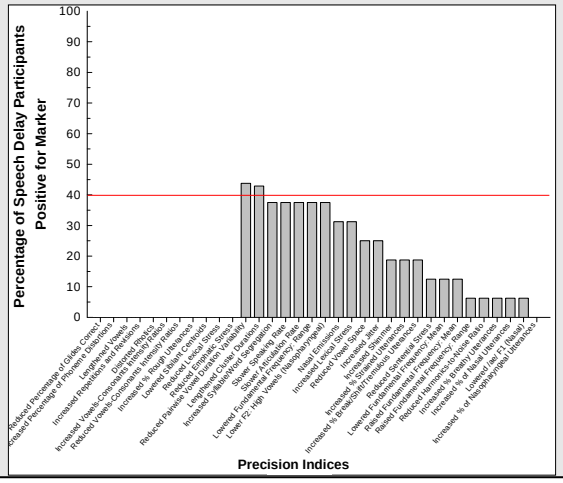
Methodological Constraints: Children with Speech Delay are 'Positive' on Many Putative Markers of CAS



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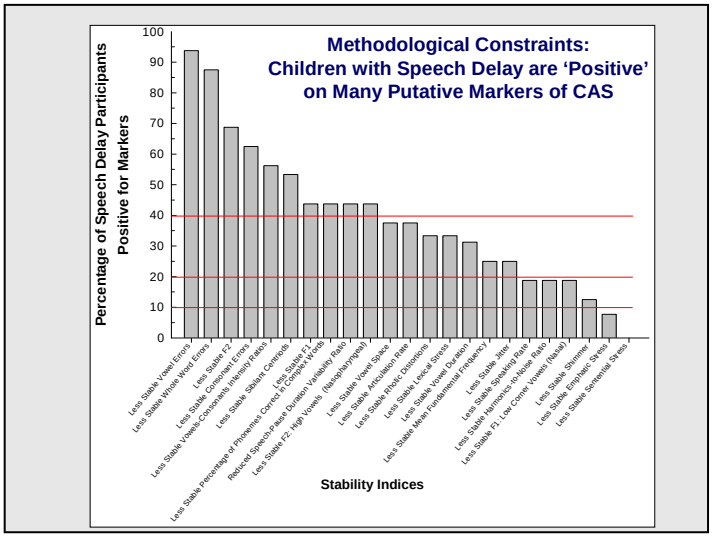

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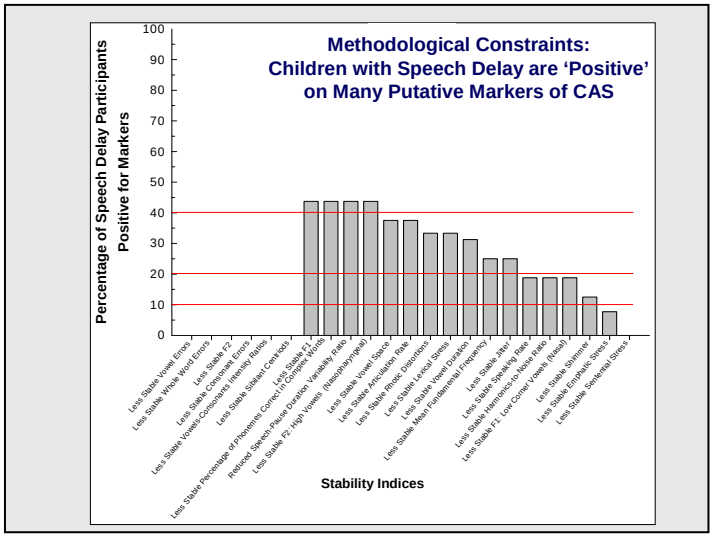

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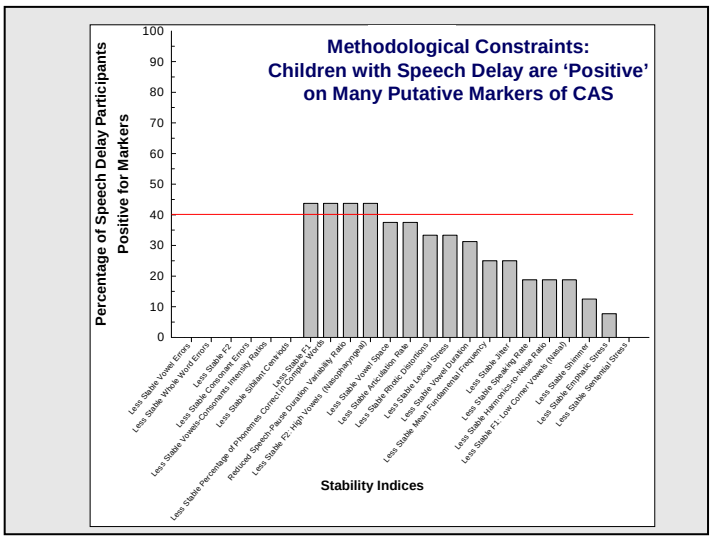

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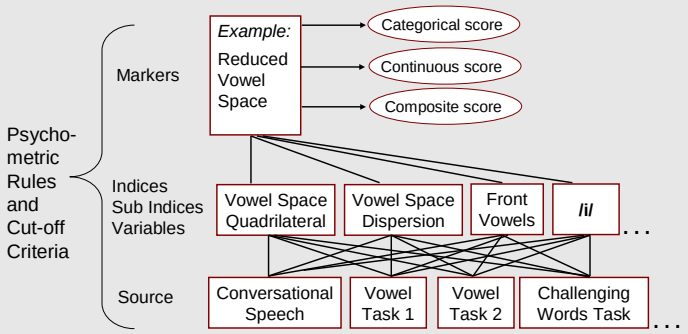
Competence, Precision, and Stability Analytics: Psychometric Structures



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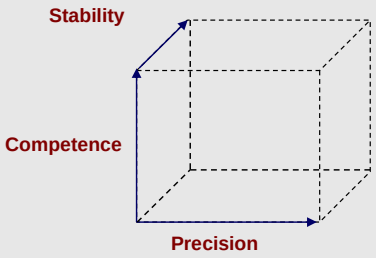
Competence, Precision, and Stability Protocol (CPSA): Current and Future Analyses



Current analyses: Box score tallies (i.e., % Positive Markers for each participant and averaged over participant groups and subgroups.)

Future analyses: Multivariate modeling (e.g., cluster analyses, structural equation analyses)

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   - B. Group and Subgroup Comparisons

IV. Discussion

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‘Top 7’ Potential Diagnostic Markers of CAS for 16 Participants with Idiopathic CAS

Domain	Index[a]	Analytic: Precision	Analytic: Stability	Diagnostic Accuracy: Effect Size[b]	Diagnostic Accuracy: 90% Confidence Interval	Diagnostic Accuracy: Sensitivity	Diagnostic Accuracy: Specificity
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**

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

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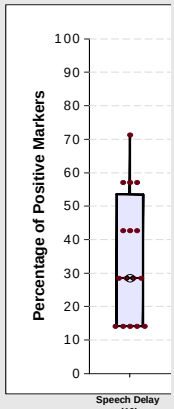
Percentage of Positive Markers (‘Top 7 Indices’) for Participants in the Study Groups and Subgroups



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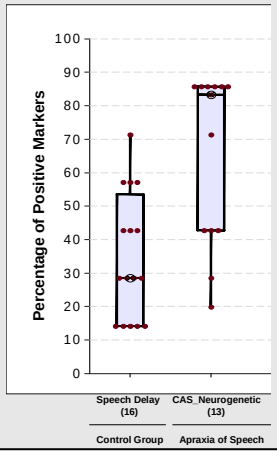
Percentage of Positive Markers (‘Top 7 Indices’) for Participants in the Study Groups and Subgroups



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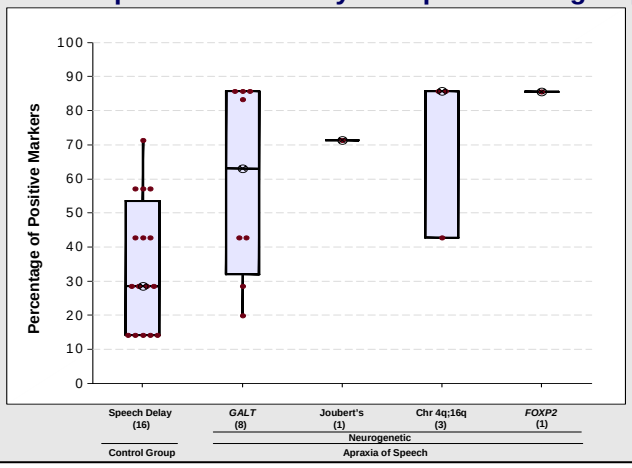
Percentage of Positive Markers (‘Top 7 Indices’) for Participants in the Study Groups and Subgroups



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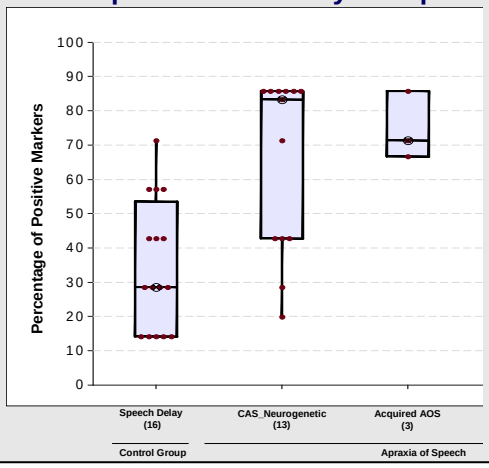
Percentage of Positive Markers (‘Top 7 Indices’) for Participants in the Study Groups and Subgroups



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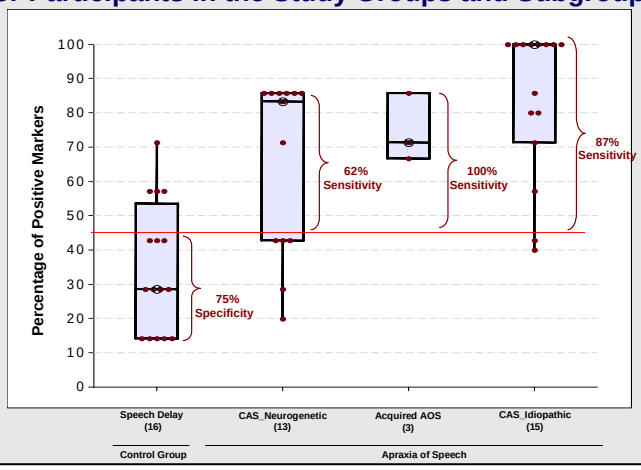
Percentage of Positive Markers ('Top 7 Indices') for Participants in the Study Groups and Subgroups



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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

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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.

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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.

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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

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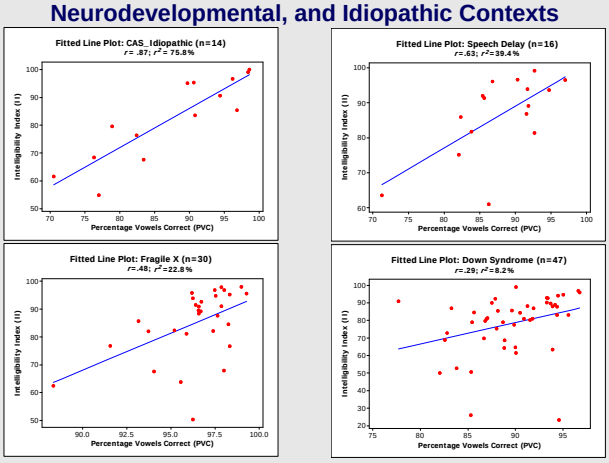
Current Research Focus: Vowel Productions in Participants with CAS in Neurologic, Neurodevelopmental, and Idiopathic Contexts



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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.

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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?

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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).

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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?

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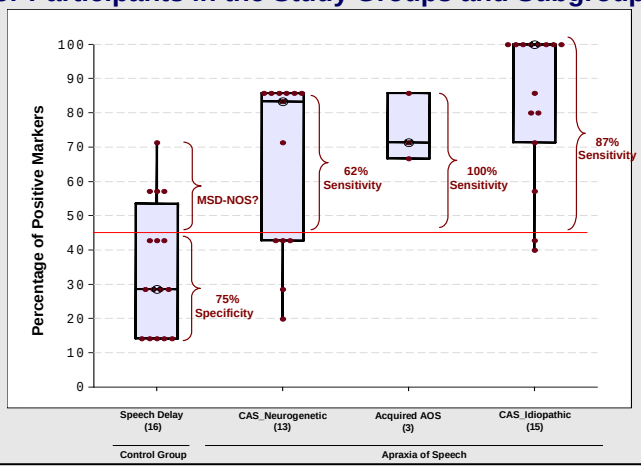
Percentage of Positive Markers ('Top 7 Indices') for Participants in the Study Groups and Subgroups



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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

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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)

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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
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IV. Discussion

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