A Diagnostic Marker to Discriminate Childhood Apraxia of Speech From Speech Delay

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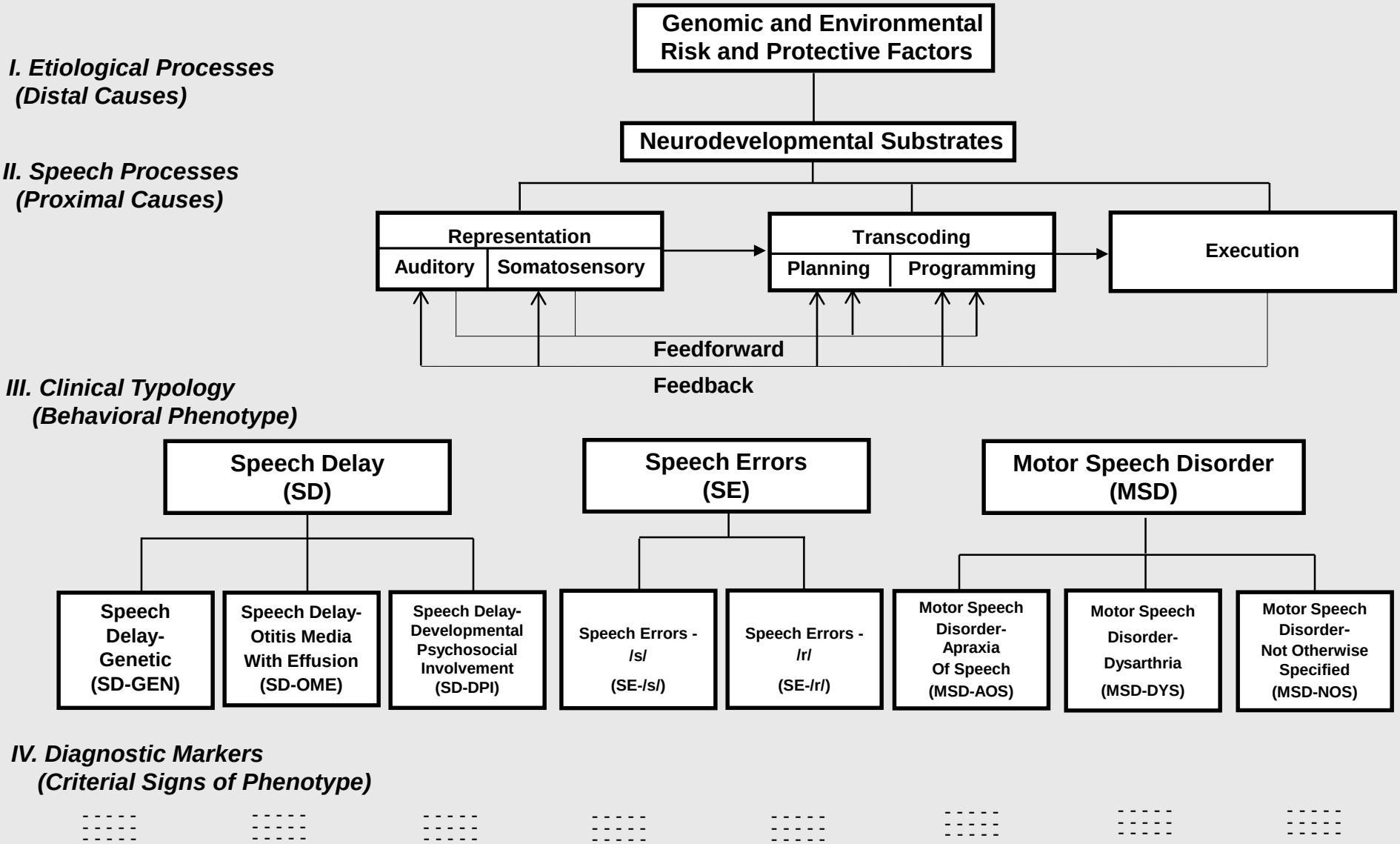
Premises

- Both Childhood Apraxia of Speech (CAS) and Speech Delay (SD) are characterized by delays in auditory and somatosensory representational and feedback processes (Shriberg, Lohmeier et al. 2012).

- CAS is characterized by additional deficits in transcoding (planning/programming) and feedforward processes.

- A highly valued diagnostic marker of CAS requires conclusive psychometric support for one cross-linguistic, lifespan sign that identifies and quantifies the transcoding and feedforward deficits.

Speech Disorders Classification System (SDCS)[a]



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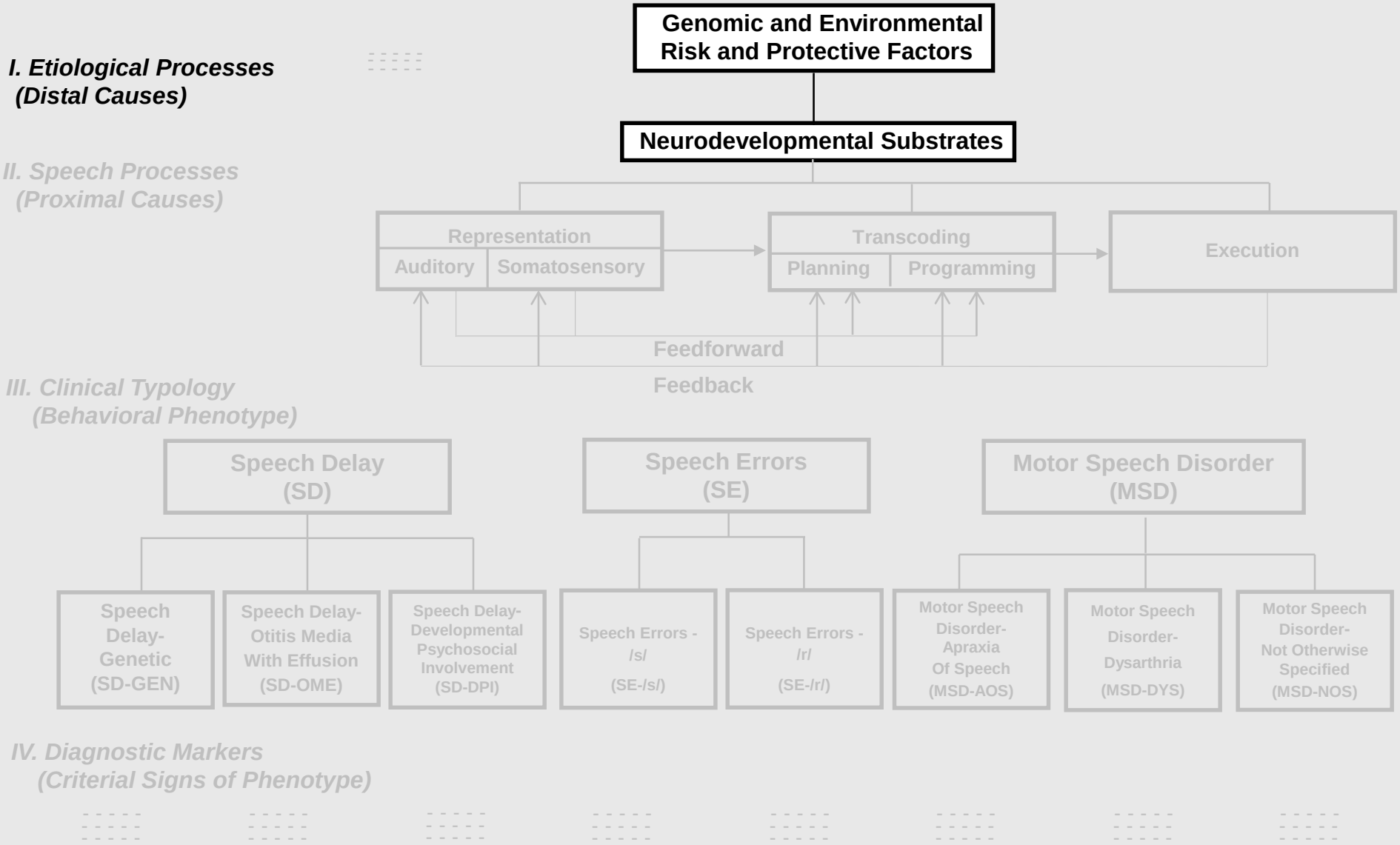

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Two Frameworks to Integrate Signs of SD and CAS With Their Genomic and Neurodevelopmental Substrates[a]

- Dual Stream Neurodevelopmental Framework
  - Focus on ventral and dorsal substrates of speech processing in CAS (Hickok, Poeppel, & colleagues, others [see References])

Neurodevelopmental Substrates of CAS Cast Within a Dual Stream Framework

Ventral Stream	Dorsal Stream
Earlier Ontogeny	Later Ontogeny
Auditory	Somatosensory
Perception	Production
Phonemic	Phonetic
Semantic, Syntactic	Articulatory
Instantiated	Novel

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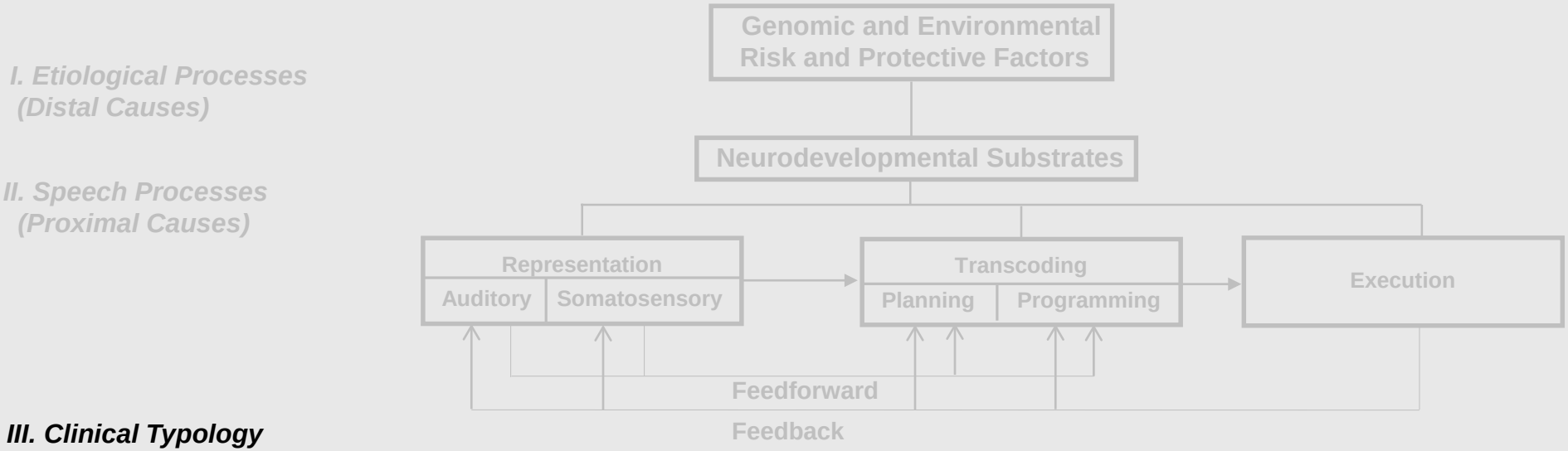
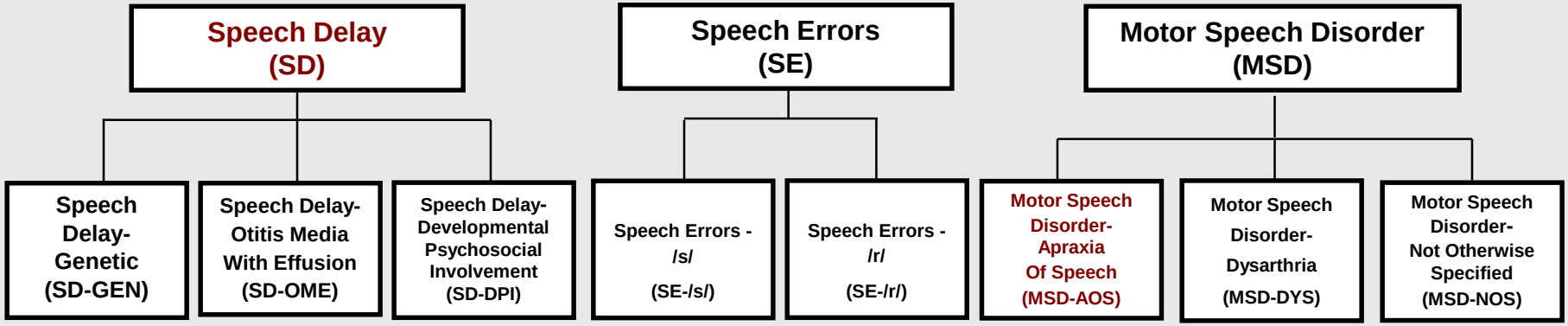
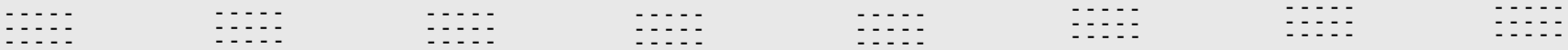


III. Clinical Typology
(Behavioral Phenotype)



IV. Diagnostic Markers
(Criterial Signs of Phenotype)



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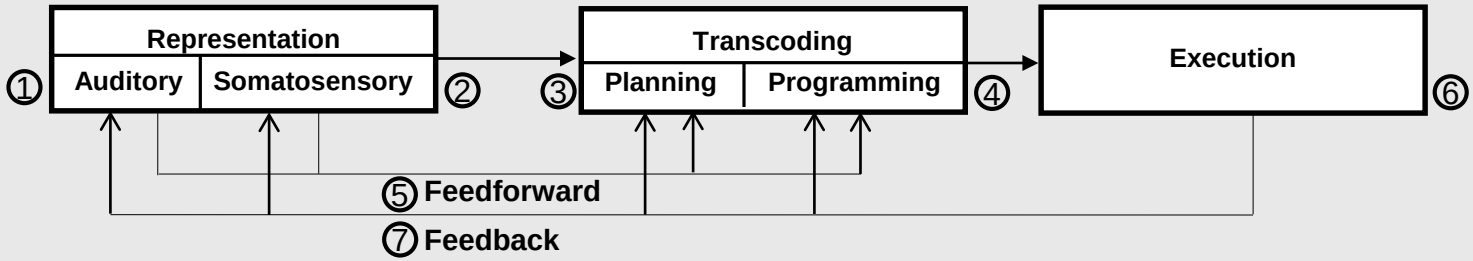
- Generic Speech Processing Framework
  - Seven-element, significantly underspecified framework (Friederici, Guenther, Hickok, Levelt, Maassen, Nijland, Poeppel, Preston, Terband, van de Merwe, Ziegler, others [see References])

II. Speech Processes (Proximal Causes)



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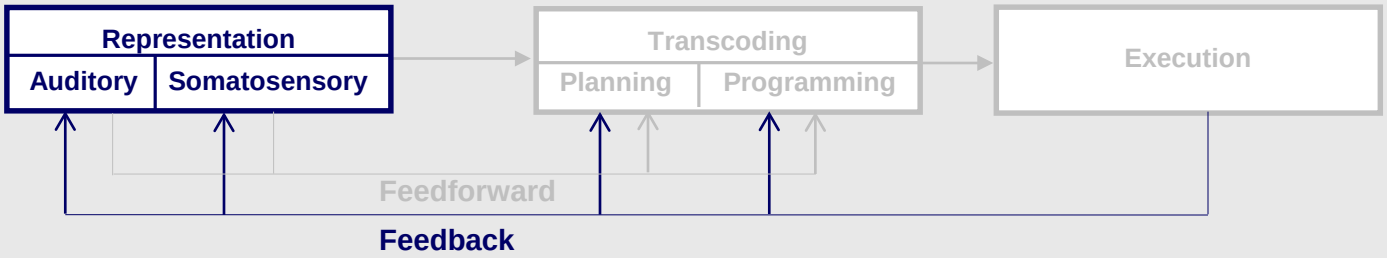

SD and CAS

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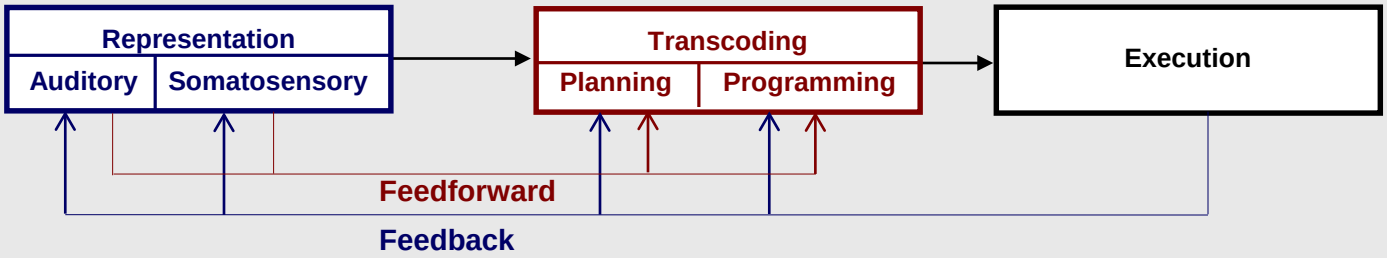

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Speculative Integration of Four Candidate Signs of CAS with the Dual Stream and Speech Processes Frameworks[a]

SDCS Level I			SDCS Level II		SDCS Levels III & IV			
Dual Stream Framework			Speech Processes Framework		Four Signs of CAS			
Ventral	Dorsal				Rate	Pauses	Stress	Transcoding
X			Representation		X	X	X	X
X			Planning		X	X	X	X
X	X		Programming		X	X	X	
X	X		Feedforward		X	X	X	
	X		Execution		X			
X	X		Feedback		X			

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('Seven Attributes of')
Highly Valued Diagnostic Markers[a]

Construct	Premise	Rationale
Accuracy	The higher the diagnostic accuracy of a diagnostic marker the more highly valued in research and clinical settings.	Diagnostic markers deemed conclusive for a disorder require >90% sensitivity and >90% specificity, yielding positive and negative likelihood ratios of at least 10.0 and at most .10, respectively.
Reliability	The higher the reliability of a diagnostic marker the more highly valued in research and clinical settings.	Reliable diagnostic markers have robust point-by-point intrajudge and interjudge data reduction agreement and internal and test-retest stability of scores, each estimated across relevant participant heterogeneities.
Coherence	The greater the theoretical coherence of a diagnostic marker the more highly valued in research and clinical settings.	As portrayed in Figure 1, conclusive diagnostic markers (Level IV) for each of the putative SSD subtypes (Level III) are highly valued for integrative descriptive-explanatory accounts when tied to their genomic, environmental, and developmental neurocognitive and sensorimotor substrates (Levels I and II).
Discreteness	Diagnostic markers from discrete, on-line events are more highly valued than diagnostic markers derived from off-line tallies of events.	Behavioral signs that that can be spatiotemporally associated with neurological events have the potential to inform explanatory accounts of speech processing deficits and identify biomarkers.
Parsimony	The fewer the number of signs in a diagnostic marker the greater its theoretical parsimony and psychometric robustness.	Each sign required for a diagnostic marker adds theoretical complexity and requires additional (multiplicative) psychometric stability.
Generality	The more extensive the generality of a diagnostic marker the more highly valued in research and clinical settings.	Diagnostic markers with the most extensive external validity may be used to identify risk for future expression of disorders, identify active expression of a disorder, and postdict prior disorder.
Efficiency	The greater the efficiency of a diagnostic marker the more highly valued in research and clinical settings.	More highly valued markers require the fewest tasks, equipment, examiner proficiencies and participant accommodations and the least time and costs to administer, score, and interpret.

[a]Shriberg et al. (2014). *A pause marker to discriminate Childhood Apraxia of Speech from Speech Delay*. Manuscript in preparation. The seven constructs are listed in their estimated rank order of importance.

Participants

Group	Cohort	Title	*n*	Age (yrs)			% Males	Percentage of Consonants Correct (PCC)		
				M	SD	Range		*M*	SD	Range
Suspected Childhood Apraxia of Speech (CAS)	Idiopathic CAS	CASI	41	8.7	4.1	4 – 23	65.9	76.6	13.5	36.8 – 98.4
	Neurogenetic CAS [a]	CASN	23	10.6	4.8	4 – 25	47.8%	75.8	12.3	44.9 – 92.2
		Total	64	9.3	4.4	4 – 25	59.4%	76.4	13.0	36.8 – 98.4
Adult-onset Apraxia of Speech (AAS)	Apraxia of Speech	AOS	14	62.1	10.9	45 – 82	78.6	91.6	7.4	68.9 – 99.4
	Primary Progressive AOS	PPAOS	16	72.4	9.1	53 – 84	56.3	92.4	6.1	74.0 – 97.9
		Total	30	67.6	11.1	45 – 84	66.7	92.0	6.7	68.9 – 99.4
Speech Delay (SD)	Clinical Cohort	SD1	88	4.3	1.3	3 – 9	73.0	72.4	12.9	17.5 - 99.1
	Research Cohort	SD2	23	5.5	0.6	5 – 7	72.7	81.8	7.3	62.7 - 91.3
	Research Cohort	SD3	84	3.9	0.7	3 – 5	71.4	69.6	9.8	36.2 - 87.2
	Research Cohort	SD4	30	4.5	0.9	3 – 7	48.3	68.8	11.4	42.1 – 82.8
		Total	225	4.3	1.1	3 – 9	69.2	71.8	11.7	17.5 – 99.1

[a] Includes participants with copy number variants (n=11) identified in related research, and participants with neurodevelopmental disorders associated with disruptions in *FOXP2* (n=4), 4q;16q translocation (n=3), 16p11.2 microdeletion syndrome (n=2), terminal deletion of chromosome 22 (n=1), Joubert syndrome (n=1), and Prader Willi syndrome (n=1).

Madison Speech Assessment Protocol (MSAP)

Four age-based protocols:

Preschool, school-aged, adolescent, adult

Each protocol includes 15 speech tasks

- Articulation Task
- Challenging Word Tasks (2)
- Challenging Phrase Task
- Consonants Task
- Conversational Sample
- DDK Task
- Phonation Task
- Syllable Repetition Tasks (2)
- Stress Tasks (2)
- Vowel Tasks (3)

Gold Standard: CAS Classifications Using a Pediatric Adaptation of the Mayo Clinic System (MCS)[a]

Classification of a speaker as positive for CAS (CAS+) requires at least 4 of the following 10 signs in at least 3 speech tasks:

- vowel distortions
- difficulty achieving initial articulatory configurations or transitionary movement gestures
- equal stress; lexical or phrasal stress errors
- distorted substitutions
- syllable or word segregation
- groping
- intrusive schwa
- voicing errors
- slow speech rate and/or slow DDK rates
- increased difficulty with multisyllabic words

[a]Dr. Strand provided written anecdotal comments on the sources and rationale for each classification.

Pause Marker (PM) Method

1. Transcribe and prosody-voice code 24 utterances from a conversational speech sample

2. Complete acoustics-aided procedures to identify occurrences of eight types of inappropriate between-word pauses in each utterance:

   Type I pauses: *abrupt, change, grope, other*

   Type II pauses: *addition, repetition/revision, long, breath*

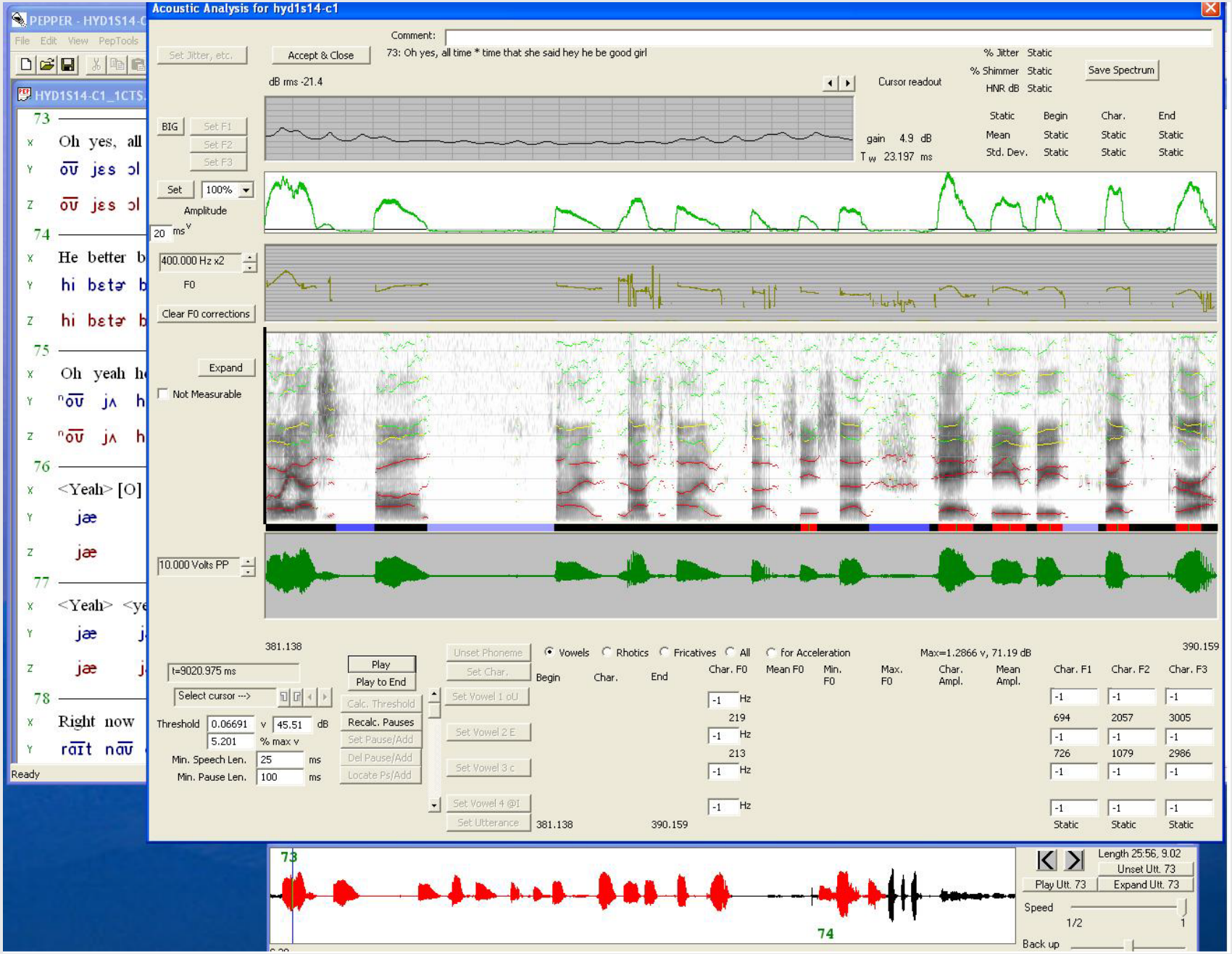
3. Calculate PM percentage:

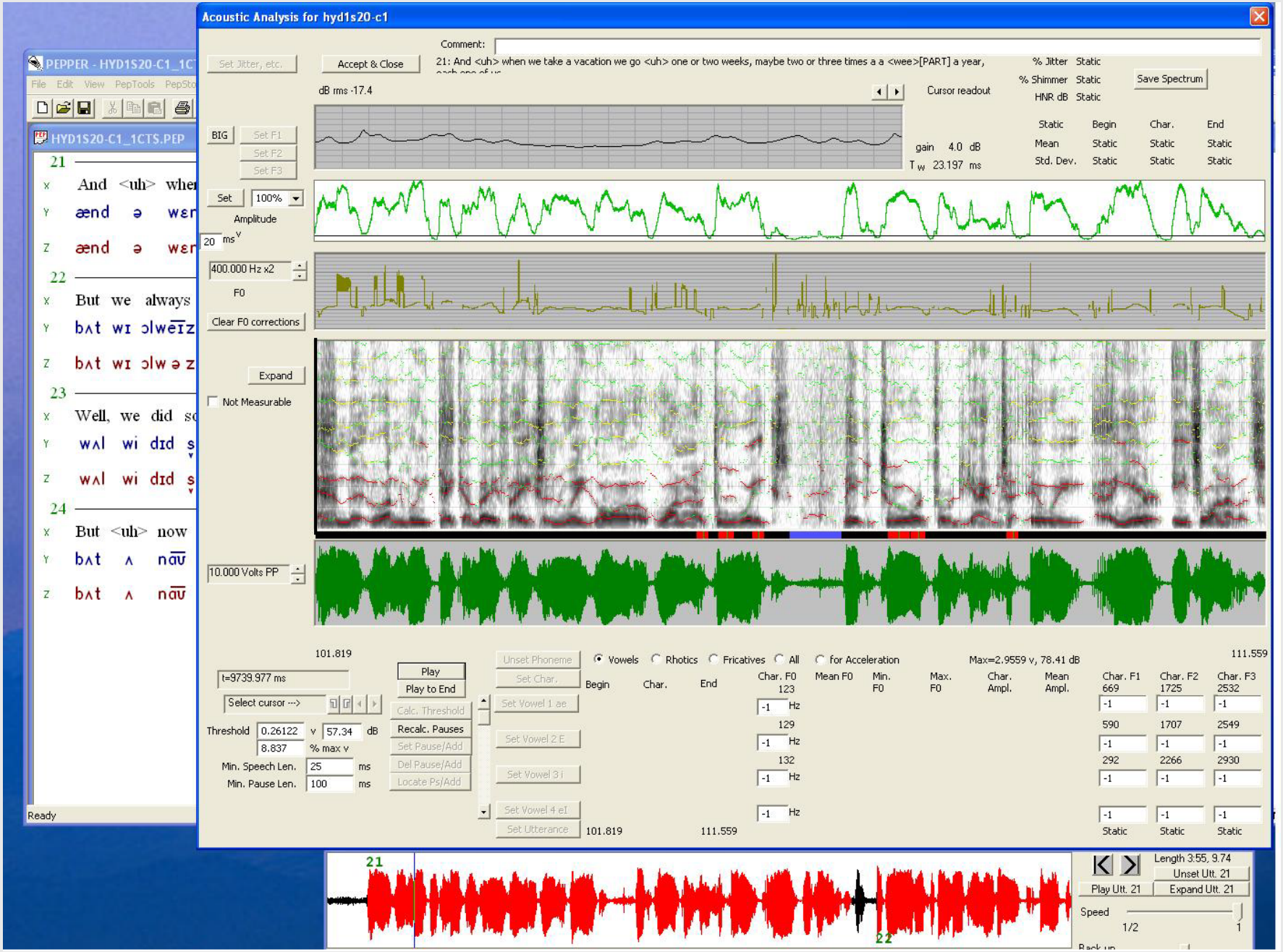
   100 x (1 – No. Type I Pauses/No. Pause Opportunities)

   where No. Pause Opportunities = No. words - No. utterances

4. Criterion for CAS+: PM < 95%[a]

[a]CAS+ classification for marginal PM scores (94.5% – 95.5%) requires positive findings on at least two of three supplementary standardized signs of CAS (Slow Articulatory Rate, Inappropriate Sentential Stress, Transcoding Errors).


PEPPER - HYD1S14-C
File Edit View PepTools
HYD1S14-C1_1CTS
73
Oh yes, all
He better b
74
Oh yeah h
75
<Yeah> [O]
76
<Yeah> <ye
77
Right now
78
Ready
Acoustic Analysis for hyd1s14-c1
Comment:
73: Oh yes, all time * time that she said hey he be good girl
Set Jitter, etc.
Accept & Close
% Jitter Static
% Shimmer Static
HNR dB Static
Save Spectrum
dB rms -21.4
Cursor readout
gain 4.9 dB
Tw 23.197 ms
Static Begin Char. End
Mean Static Static Static
Std. Dev. Static Static Static
BIG
Set F1
Set F2
Set F3
Set
100%
Amplitude
20 ms
400.000 Hz x2
F0
Clear F0 corrections
Expand
Not Measurable
10.000 Volts PP
381.138
t=9020.975 ms
Select cursor --->
Play
Play to End
Calc. Threshold
Recalc. Pauses
Set Pause/Add
Del Pause/Add
Locate Ps/Add
Threshold 0.06691 v 45.51 dB
5.201 % max v
Min. Speech Len. 25 ms
Min. Pause Len. 100 ms
Unset Phoneme
Set Char.
Set Vowel 1 oU
Set Vowel 2 E
Set Vowel 3 c
Set Vowel 4 @I
Set Utterance
Vowels Rhotics Fricatives All for Acceleration
Max=1.2866 v, 71.19 dB
390.159
Begin Char. End Char. F0 Mean F0 Min. F0 Max. F0 Char. Ampl. Mean Ampl. Char. F1 Char. F2 Char. F3
Hz
219
213
694 2057 3005
726 1079 2986
Static Static Static
73
74
Length 25:56, 9.02
Unset Utt. 73
Play Utt. 73
Expand Utt. 73
Speed
1/2
1
Back up


PEPPER - HYD1S20-C1_1CT
File Edit View PepTools PepSto
HYD1S20-C1_1CTS.PEP
21
x And <uh> wher
y æ n d ə w ɛ r
z æ n d ə w ɛ r
22
x But we always
y b ʌ t w ɪ ɔ l w eɪ z
z b ʌ t w ɪ ɔ l w ə z
23
x Well, we did s
y w ʌ l w i d ɪ d s
z w ʌ l w i d ɪ d s
24
x But <uh> now
y b ʌ t ʌ n aʊ
z b ʌ t ʌ n aʊ
Ready
Acoustic Analysis for hyd1s20-c1
Comment:
Set Jitter, etc.
Accept & Close
21: And <uh> when we take a vacation we go <uh> one or two weeks, maybe two or three times a a <wee>[PART] a year,
% Jitter Static
% Shimmer Static
HNR dB Static
Save Spectrum
dB rms -17.4
Cursor readout
BIG
Set F1
Set F2
Set F3
gain 4.0 dB
T w 23.197 ms
Static Begin Char. End
Mean Static Static Static
Std. Dev. Static Static Static
Set
100%
Amplitude
20 ms
400.000 Hz x2
F0
Clear F0 corrections
Expand
Not Measurable
10.000 Volts PP
101.819
t=9739.977 ms
Select cursor --->
Threshold 0.26122 v 57.34 dB
8.837 % max v
Min. Speech Len. 25 ms
Min. Pause Len. 100 ms
Play
Play to End
Calc. Threshold
Recalc. Pauses
Set Pause/Add
Del Pause/Add
Locate Ps/Add
Unset Phoneme
Set Char.
Set Vowel 1 ae
Set Vowel 2 E
Set Vowel 3 i
Set Vowel 4 eI
Set Utterance
101.819
111.559
Vowels Rhotics Fricatives All
for Acceleration
Max=2.9559 v, 78.41 dB
111.559
Begin Char. End Char. F0 Mean F0 Min. F0 Max. F0 Char. Ampl. Mean Ampl. Char. F1 Char. F2 Char. F3
123 669 1725 2532
129 590 1707 2549
132 292 2266 2930
Hz
Static Static Static
21
22
Length 3:55, 9.74
Unset Utt. 21
Play Utt. 21
Expand Utt. 21
Speed
1/2
1
Back up

Procedures to Resolve MCS-PM Classification Disagreements

1. Assembled best estimates of 'true positive' and 'true negative' CAS groups:
   - Consensus CAS+ Group (n = 35):

     participants classified CAS+ by both diagnostic markers
   - Consensus CAS- Group (n = 15):

     participants classified CAS- by both diagnostic markers

2. Computed descriptive and inferential statistics for relevant demographic and speech variables for and between the two CAS consensus groups; compared findings for each disagreement to findings for the two CAS consensus groups

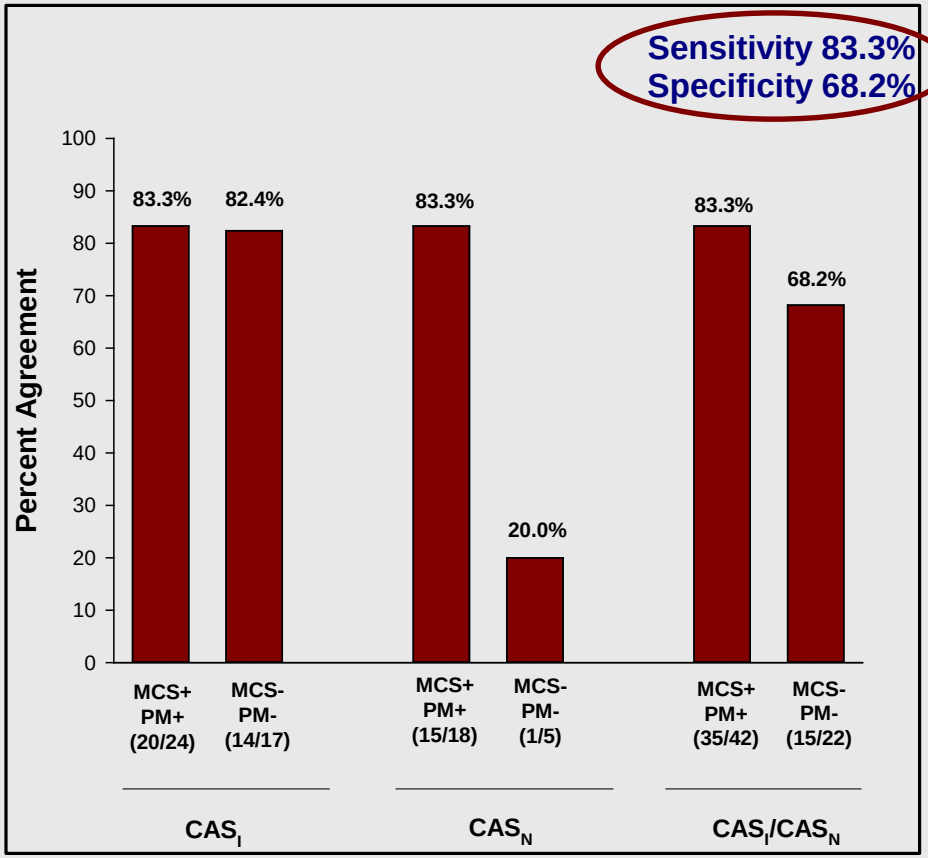
Procedures to Resolve MCS-PM Classification Disagreements

3. Determined case-by-case support for resolving each MCS-PM classification disagreement as either due to conceptual differences in MCS vs. PM criteria for CAS+, or as 'questionable' due to either method constraints (e.g., insufficient MSAP data) and/or statistical support consistent with the alternative Consensus CAS group

4. Recalculated the estimated diagnostic accuracy of the PM with all 'questionable' disagreements excluded.

MCS-PM Classification Agreement Findings: 64 Participants Suspected Positive for CAS

Includes 7 Participants with 'Questionable' MCS+PM- Classifications



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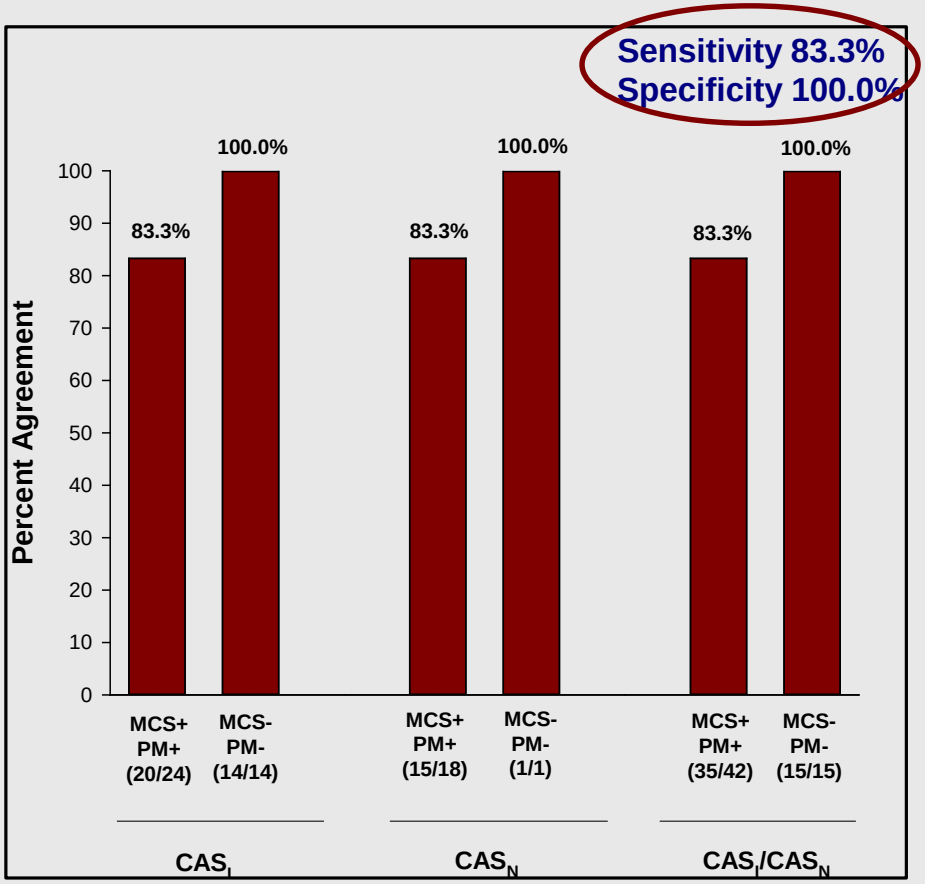
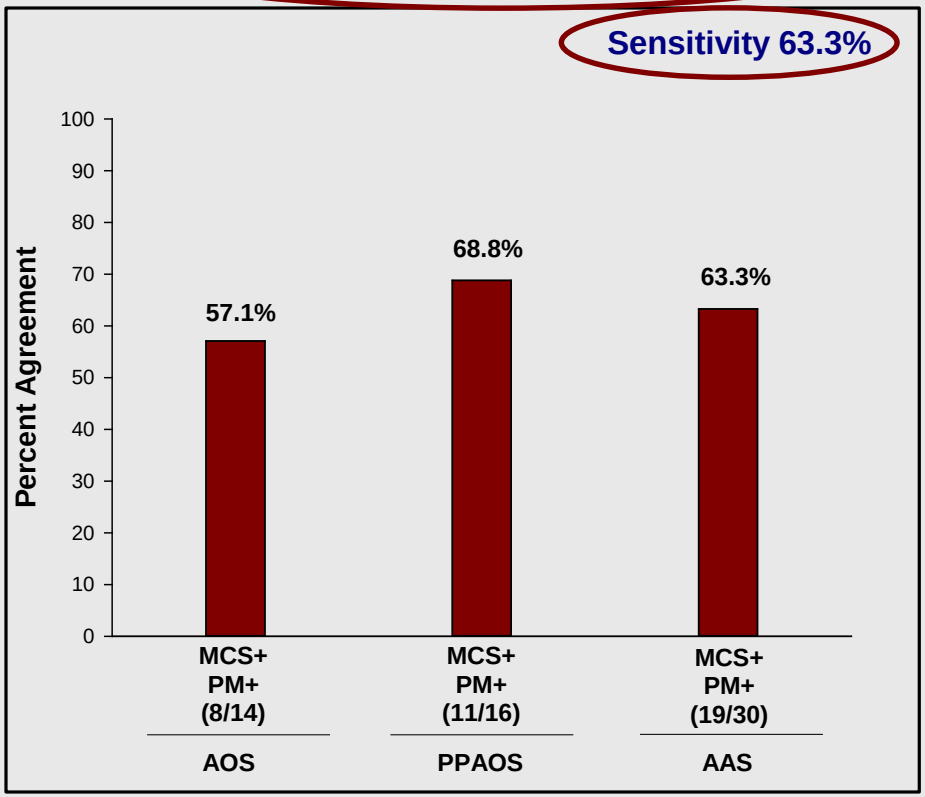


MCS-PM Classification Agreement Findings: 30 Participants with AAS (AOS and PPAOS)

Includes 11 Participants termed "Voicers"



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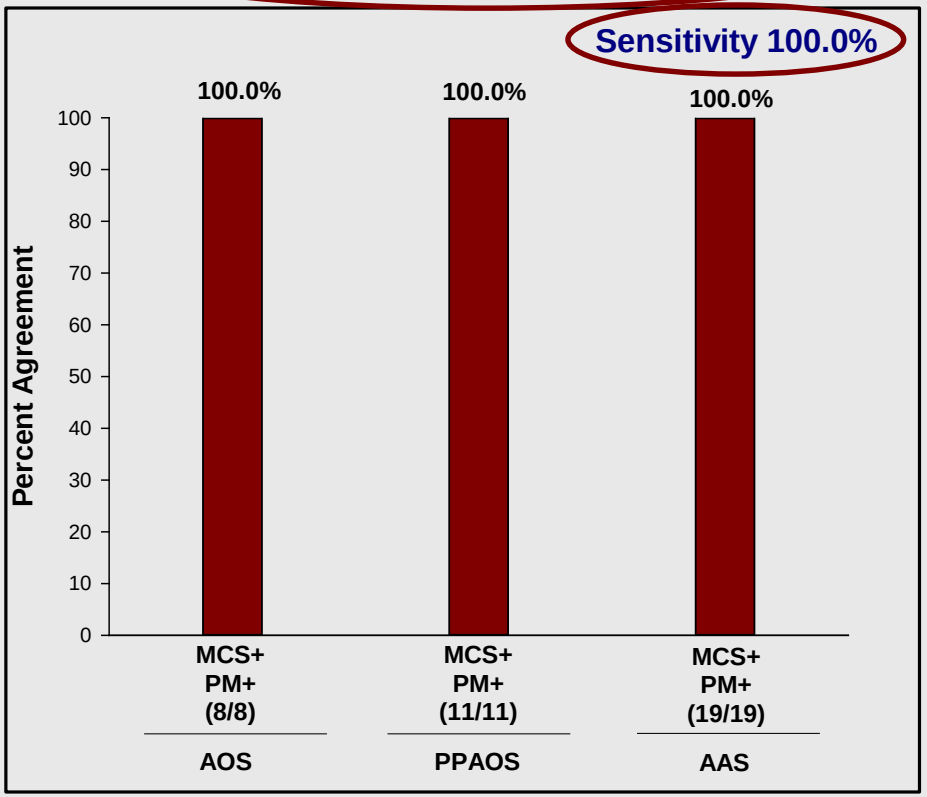
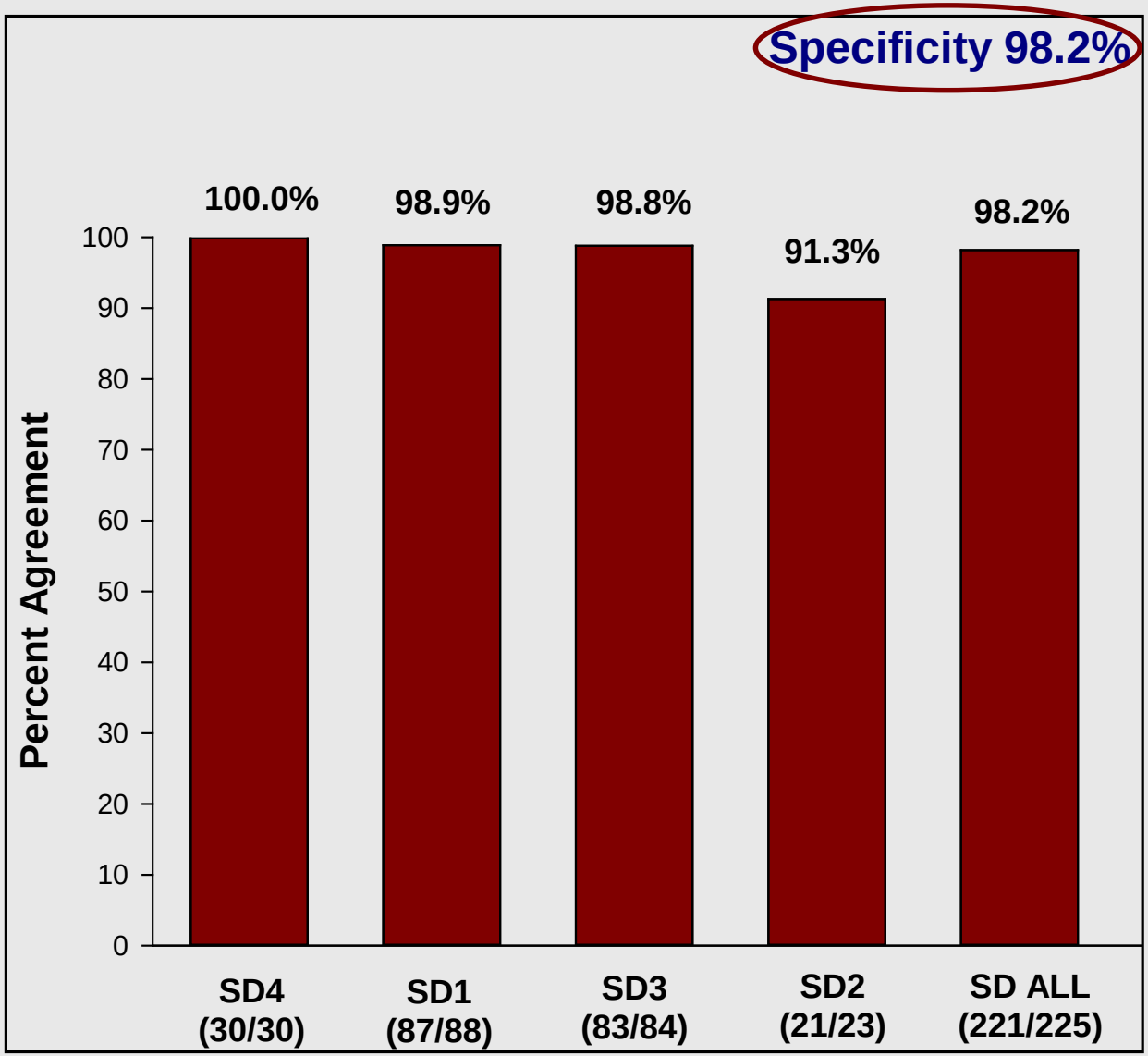


SDCS-PM Classification Agreement Findings: 225 Participants with Speech Delay



Conclusions

- The PM provides a single-sign marker that likely can be used cross-linguistically to discriminate CAS from SD, and to scale the severity of CAS.

- The Type I pauses identified and quantified by the PM have theoretical 'Coherence.' The claim is that these atypical cessations of continuous speech are consequent to deficits in planning, programming, and/or feedforward processes.

- PM findings are interpreted to meet six of the seven proposed criteria for a highly valued diagnostic marker of CAS, requiring additional research to improve 'Efficiency. '

Research Directions

Methodological

- Cross-validate the current, estimates of intrajudge and interjudge reliability of the PM (low-to mid 80%)
- Cross-validate the current acoustic correlate (steep amplitude rise time) of the most frequent type of inappropriate pause (Type I: '*abrupt*') and explore automated detection of '*abrupt* ' pauses
- Develop alternatives to continuous speech samples for speakers suspected positive for CAS who have limited verbal output
- Assess the specificity of the PM for speakers with different types of dysarthria

Research Directions

Substantive

- Assess the informativeness of the PM in collaborative neuroscience studies to explicate the genomic and neural correlates of planning, programming, and feedforward deficits in CAS and AAS toward a biomarker of apraxia of speech.

- Assess the utility of the PM in collaborative studies to characterize normalization processes in CAS and to quantify treatment efficacy in studies of CAS and AAS.

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