# Neuroimaging of Children with Speech Sound Disorders

Barbara Lewis Jonathan Preston Erin Redle Jennifer Vannest Lawrence Shriberg

### **Outline of Presentation**

- Introduction to the Session- Dr. Lewis
- Basic Principles of fMRI Dr. Vannest
- Study 1:
  - Overview, participants, and paradigms Dr. Redle
  - Madison CAS Phenotype Dr. Shriberg
  - FMRI Study Results- Dr. Vannest
- Study 2: Dr. Preston
- Questions and Panel Discussion- All

### **Session Introduction**

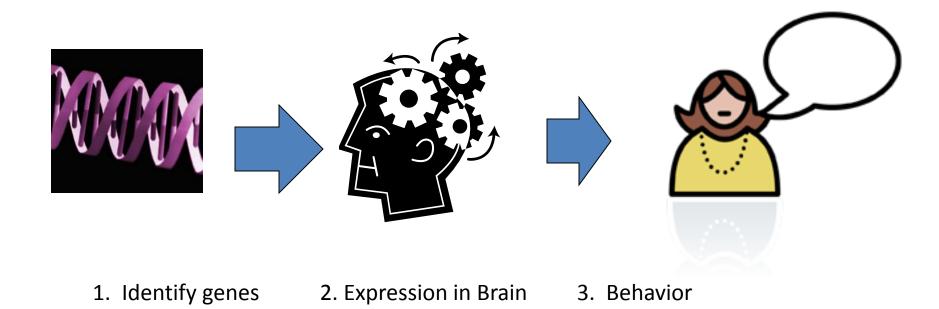
**Neuroimaging of Children With Speech Sound Disorders** 

American Speech-Language-Hearing Association National Convention, Atlanta, GA November 16, 2012

> Barbara Lewis, Ph.D. CCC-SLP Professor, Communication Sciences Case Western Reserve University bxl@case.edu



### **Imaging Genetics**



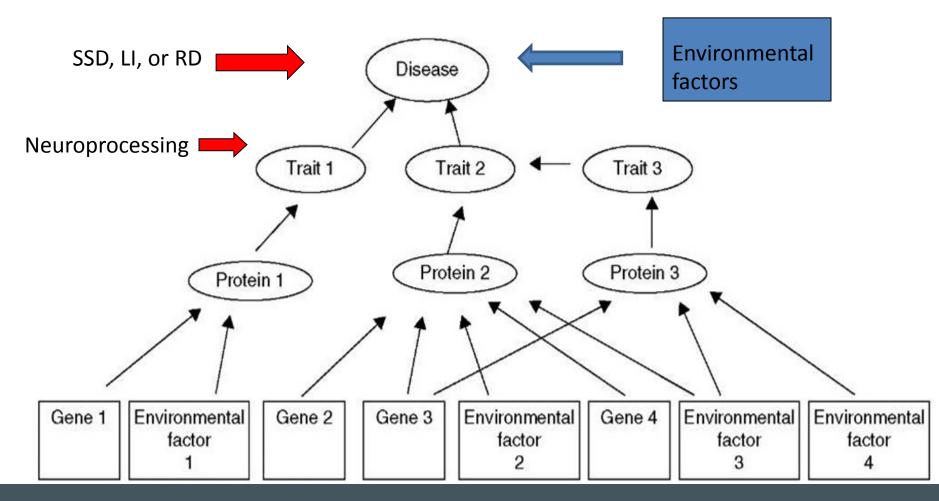


### The Emerging Field of Imaging Genetics

- Imaging genetics is the use of imaging technology as a phenotype to evaluate how genes that influence disorders are expressed in the brain.
- Both genetics and environment are important in determining brain function. Integrating genetics with neuroimaging will improve our understanding of speech and language disorders.
- There is a need for novel analytic, statistical and visualization techniques.

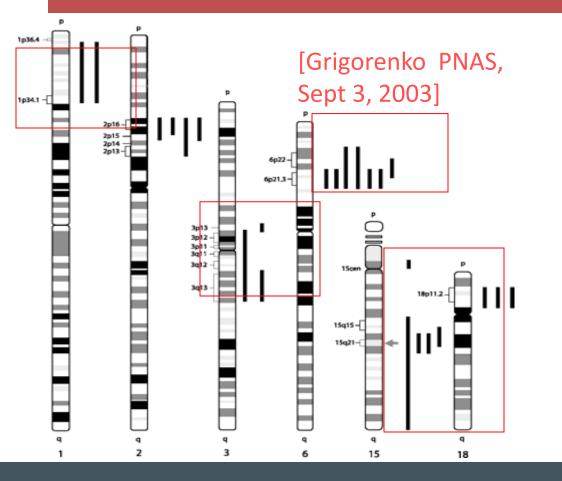


### Genetic Architecture of a Complex Trait





### Scope of the problem



•Is there a link between speech sound and language disorders and dyslexia?

•Chromosomes 1, 3, 6, 15



### Linkage Results for Spoken Language and Written Expression (Lewis et al., 2011)

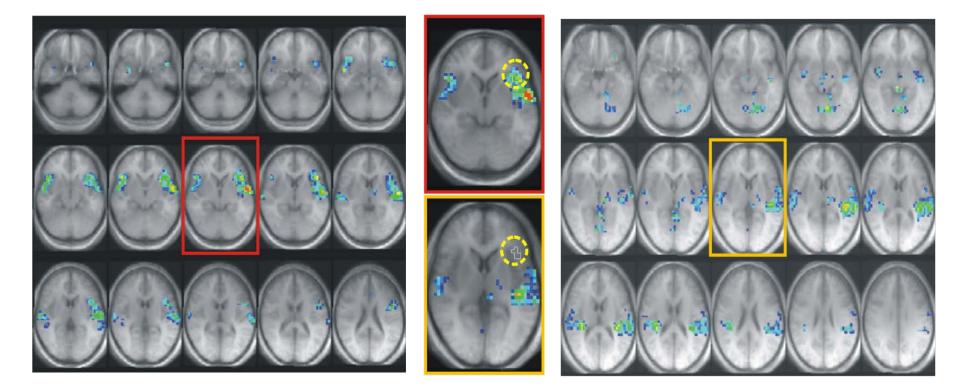
Chromosome	Spoken Language at Early Childhood	Written Expression at School-age
Chromosome 1	Articulation	Written vocabulary
	Vocabulary	Reading decoding
	Phon. Memory	Spelling
Chromosome 3	Articulation	Written vocabulary
	Vocabulary	Spelling
	Phon, Memory	Reading decoding
	Speeded Naming	
Chromosome 6	Vocabulary	Spelling
	Phon. Memory	
Chromosome 15	Oral Motor	Reading decoding
	Articulation	Spelling
	Phonological Memory	



# What are specific genes that may underlie speech sound disorders?

- FOXP2: Located on 7q13; a brain expressed transcription factor that affects brain development; identified in the KE family (Liegeios et al., 2003).
- ROBO1 and ROBO2: Located on chromosome 3; guides axons and influences neuronal axon growth; identified in dyslexics in Finland (Nopola-Hemmi et al., 2001).
- KIAA0319, TTRAP, and DCDC2: Located on chromosome 6; genes disrupt neuronal migration; identified in dyslexic by numerous research groups (Grigorenko et al., 2000; Smith et al., 2007).
- BDNF: Brain-derived neurotrophic factor related to nerve growth and differentiation in the brain (Stein, unpublished).
- DYX8: Region on chromosome 1 that demonstrates pleiotropy for SSD and dyslexia (Miscamarra et. al., 2007).
- Aromatase (CYP19A1): Located on 15q21.2; This gene regulates estrogen synthesis in specific brain areas. It is related to synaptic plasticity and axonal growth (Anthoni et al., 2012).





On the left, controls without a history of speech and language disorders show the expected activation in the language areas while repeating nonsense words. On the right, participants with a history of speech sound disorders show under activation of the language areas during repetition of nonsense words (Tkach et al., 2011).



# Collaborative Study with CWRU, CCHMC, and U. Of Wisconsin

- The **first objective** is to compare neural substrates used in speech motor planning and production, fine motor planning and praxis, and visual-auditory perception in children with CAS, with speech delay and with typically developing children.
- The **second objective** is to determine how well current clinical measures correlate with observed neurophysiological differences in speech motor planning and production in children with CAS, speech delay and typically developing children.
- The **third objective** is to determine how genes influence neural development result in neurological processing differences in children with CAS and speech delay as compared to typically developing children.



# **Clinical Implications**

- An improved understanding of the genetic and neurological underpinnings of CAS and speech delay will:
  - Identify the biological mechanisms that underlie both typical and disordered speech.
  - Aid in the early identification of children at risk for CAS and speech delay.
  - Facilitate the development of more specific and effective therapies.
  - Early identification and more effective therapies will result in improved long-term academic, occupational and social outcomes.



### References

- Anthoni, H., Sucheston, L.E., Lewis, B.A., Tapia-Paez, I., Fan, X., Zucchelli, M., Taipale, M., Stein, C.M. et al. (2012). The Aromatase Gene CYP19A1: Several genetic and functional lines of evidence supporting a role in reading, speech and language. *Behavior Genetics*, 42(4), 509-527.
- Grigorenko, E. L. (2003). The first candidate gene for dyslexia: Turning the page of a new chapter of research. *PNAS*, *100 (20)*, 11190-11192.
- Grigorenko, E.L., Wood, F.B., Meyer, M.S., Hart, & Pauls, D.L. (2000). Chromosome 6 p influences on different dyslexia related cognitive processes: further confirmation. *Journal of Human Genetics, 66,* 715-723.
- Liegeois, F., Baldeweg, T., Connelly, A., Gadian, D. G., Mishkin, M., & Vargha-Khadem, F. (2003). Language fMRI abnormalities associated with FOXP2 gene mutation. *Nat Neurosci*, 6(11), 1230-1237.
- Lewis, B., Avrich, A., Freebairn, L., Hansen, A., Sucheston, L., Kuo, I., Taylor, H.G., Iyengar, S., Stein, C. (2011).
  Outcomes of children with speech sound disorders: Impact of endophenotypes. *Journal of Speech Language and Hearing Research*, 54, 1628-1643.
- Lewis, B. A., Shriberg, L.D., Freebairn, L.A., Hansen, A.J., Stein, C.M., Taylor, H.G.& Iyengar, S.K. (2006). The genetic bases of speech sound disorders: evidence from spoken and written language. *J. Speech Lang Hear. Res.* 49, 1294-1312.
- Miscamarra, L., Stein, C.M., Millard, C., Kluge, A., Cartier, K.C., Freebairn, L.A. et al. (2007). Further evidence of pleiotropy influencing speech and language: Analysis of the DYX8 region. *Human Heridity, 63, 47-58.*
- Nopola-Hemmi, J., Myllyluoma, B., Haltia, T., Taipale, M., Ollikainen, V., Ahonen, T., et al. (2001). A dominant gene for developmental dyslexia on chromosome 3. *Journal of Medical Genetics, 38,* 658-664.



### References

- Schmithorst, V. J., & Holland, S. K. (2004). Event-related fMRI technique for auditory processing with hemodynamics unrelated to acoustic gradient noise. *Magn Reson Med*, 51(2), 399-402.
- Smith, S.D. (2007). Genes, language development, and language disorders. *Mental Retardation and Developmental Disabilities Research Reviews, 13,* 96-105.
- Stein, C. M., Schick, J.H., Taylor, G.H., Shriberg, L.D., Millard, C., Kundtz-Kluge, A. et al. (2004). Pleiotropic effects of a chromosome 3 locus on speech-sound disorder and reading. *Am. J. Hum. Genet.* 74, 283-297.
- Stein, C. M., Miller, C., Kluge, A., Miscimarra, L.E., Cartier, K.C., Freebairn, L.A. et al. (2006). Speech Sound Disorder Influenced by a Locus in 15q14 Region. *Behav. Genetics*, *36(6)*, 858-868.
- Tkach, J.A., Chen, X., Freebairn, L.A., Schmithorst, V.J., Holland, S.K., & Lewis, B.A. (i2011). Neural Correlates of Phonological Processing in Speech Sound Disorder: A Functional Magnetic Resonance Imaging Study, *Brain and Language*. *119*,42-49.



### **Basic Principles of fMRI**

**Neuroimaging of Children With Speech Sound Disorders** 

American Speech-Language-Hearing Association National Convention, Atlanta, GA November 16, 2012

Jennifer Vannest, Ph.D. Assistant Professor, Division of Neurology Assistant Director, Pediatric Neuroimaging Research Consortium Cincinnati Children's Hospital Medical Center

jennifer.vannest@cchmc.org





### **Background: Functional Imaging**

Based on the assumption that the brain is "functionally segregated"

- isolate a particular process experimentally
- examine <u>relative</u> changes in neural activity a comparison between "active" and "baseline" conditions
- E.g. listening to speech vs. listening to noise





### Magnetic Resonance Imaging (MRI)



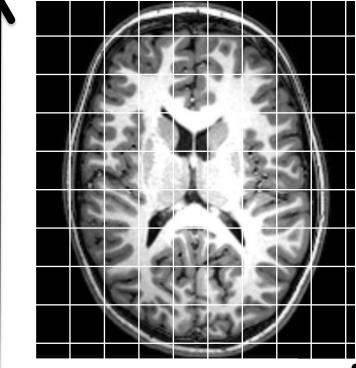
- Participant is placed in a strong magnetic field
- Radio transmitter/receiver around area to be imaged
- Safety concerns: magnetic items will be drawn to the center of the magnet
- Many other substances (especially metals) can cause distortions in images
- Electromagnetic interference in environment
- Significant acoustic noise





• White matter, grey matter and cerebrospinal fluid have 3 different magnetic properties. This allows the 3 different kinds of tissue to be separated with MRI.

Gradients in the magnetic field are used as a "grid" to localize regions of tissue

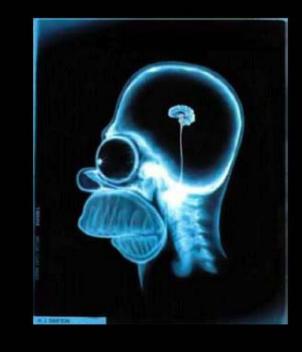






### MRI vs. fMRI

### MRI studies brain anatomy.



### Functional MRI (fMRI) studies brain function.



(From Jody Culham's fMRI for Newbies)



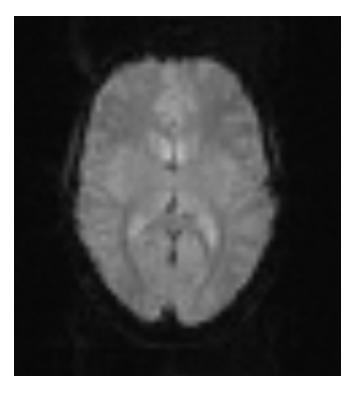
Process of interest -> Neuronal Activity -> Increased Metabolism and Bloodflow -> Increased Deoxygenated blood

Deoxygenated blood has magnetic properties and creates local changes in the magnetic field

# BOLD response: Blood Oxygen Level - Dependent







- Relatively low spatial resolution (for MRI)
- Sensitive to BOLD response
- •1 brain volume takes 2 sec to acquire
- Scan for 5-7 minutes
- Alternate between active and baseline conditions

### **Structural Data**

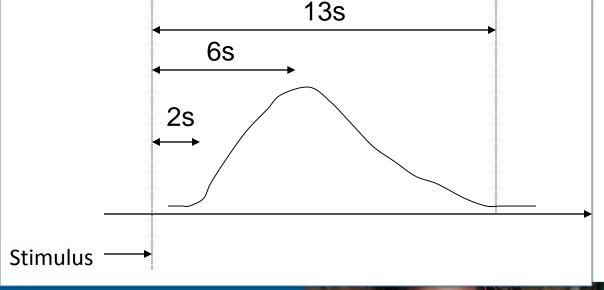
- High spatial resolution
- 1 brain volume takes 6 min to acquire



### fMRI: Experimental Design Issues

Because of the slow timing of the hemodynamic response, we try to optimize the design of fMRI experiments to be as sensitive as possible to relative increases in bloodflow.

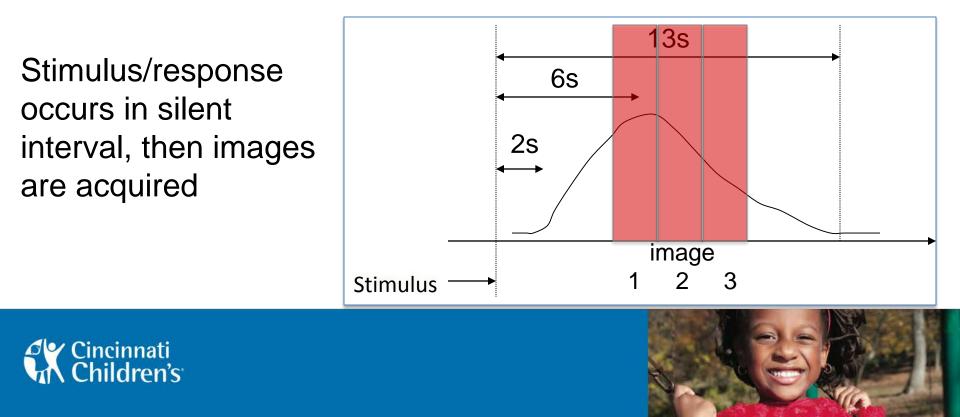
We also must take into account behavioral characteristics of the task during active and baseline conditions





### fMRI: Experimental Design Issues

"HUSH" or "Sparse" techniques take advantage of the slow timing of the hemodynamic response



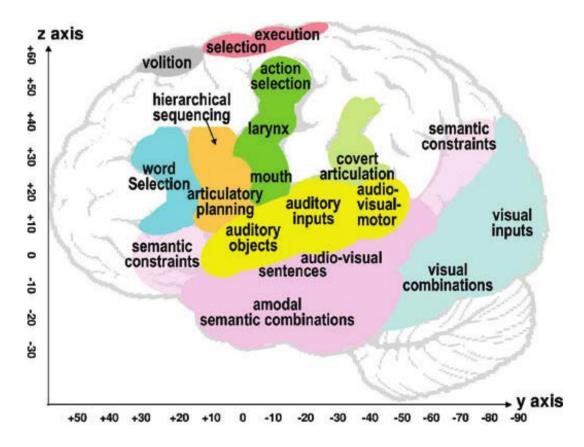
### fMRI: Data Analysis

- Motion correction
- Group analysis
  - Normalize all participants' brains to the same size
  - Look for voxels that have consistently greater BOLD response in the active versus baseline condition across all participants (statistically significant)
  - Correction for multiple comparisons across voxels
  - BOLD response can also be correlated with a behavioral measure
  - Comparisons between groups





### fMRI: Speech and Language Networks



Price (2010) Cincinnati Children's



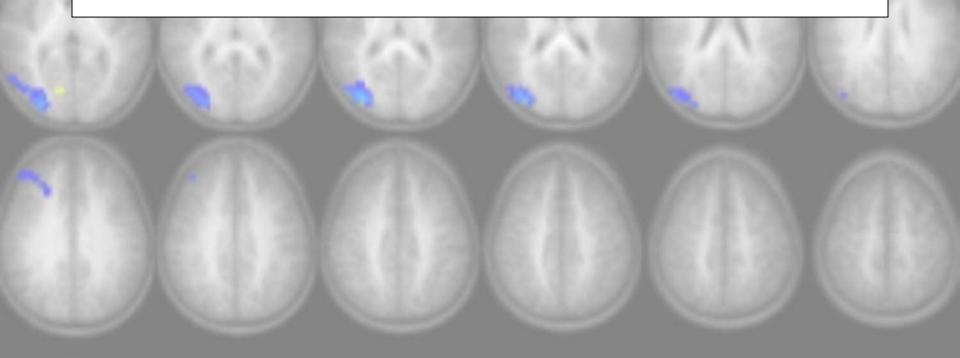
### References

- Culhman, J. (2012, January 31). fMRI 4 newbies: A crash course in brain imaging. Retrieved from <a href="http://culhamlab.ssc.uwo.ca/fmri4newbies/">http://culhamlab.ssc.uwo.ca/fmri4newbies/</a>
- Price, C.J. (2010). The anatomy of language: a review of 100 fMRI studies published in 2009. Annals of the New York Academy of Sciences, 1191, 62-88.





Study 1: Functional Magnetic Resonance Imaging (fMRI) Study of Speech Production in Childhood Apraxia of Speech



### Grants Acknowledgement

 This research was supported by grants from the National Institutes of Health, National Institute on Deafness and other Communication Disorders including DC000528, DC00496, and DC010188-02.

### **Collaborating Laboratories**

# Case Western Reserve

Barbara Lewis, PhD Lisa Freebairn, M.A. Jessica Tag, M.A. Gerry Taylor, Ph.D. Sudha Iyengar, PhD Catherine Stein, Ph.D. Allison Avrich B.S. Robert Elston, PhD Feiyou Qui, MS



• <u>University of Wisconsin</u> <u>Madison</u>

Lawrence D. Shriberg, Pl

RSITY OF WISCONSIN-MADISON



incinnati

*`hildren's* 

<u>Cincinnati Children's Hospital</u>
 <u>Medical Center</u>

FNTFR

Erin Redle, PhD Jennifer Vannest, PhD Jean Tkach, PhD Scott Holland, PhD Thomas Maloney, M.S.

VAISMAN (



Pediatric Neuroimaging Research Consortium



# Overview, Participants, and Paradigms

**Neuroimaging of Children With Speech Sound Disorders** 

#### American Speech-Language-Hearing Association National Convention, Atlanta, GA November 16, 2012

Erin E. Redle, Ph.D. CCC-SLP

Division of Speech Pathology Assistant Professor, Communication Sciences Research Center Quality Scholar, James M. Anderson Center for Health Systems Excellence Cincinnati Children's Hospital Medical Center

erin.redle@cchmc.org





## Background

- SSDs, including CAS, arise from differences in neural substrates supporting speech production
- Several neuroimaging studies of the KE family (severe SSD, FOXP2 gene mutation)
  - Structural imaging found gray matter volume differences in Broca's area, pre-supplementary motor area (SMA), the caudate nucleus, and the lentifrom nucleus in affected vs. non-affected family members (Vargha-Khadem et al., 1998)
  - Functional imaging also found differences in Broca's area during over and covert speech tasks between affected and non-affected family members (Liegeois et al., 2003)
- Tkach et al., 2011
- Preston et al., 2012
- Better understanding of disorders may lead to more targeted and more effective interventions





### Participants

- Children 5-12 years
  - Typical Speech Development (TSD)
  - Speech Sound Disorder
    - Speech Delay or Motor Speech Disorder- Not Otherwise Specified (MSD-NOS)
    - CAS
- Recruitment Sources
  - Neurodevelopmental Apraxia Clinic
  - Division of Speech Pathology
  - Community



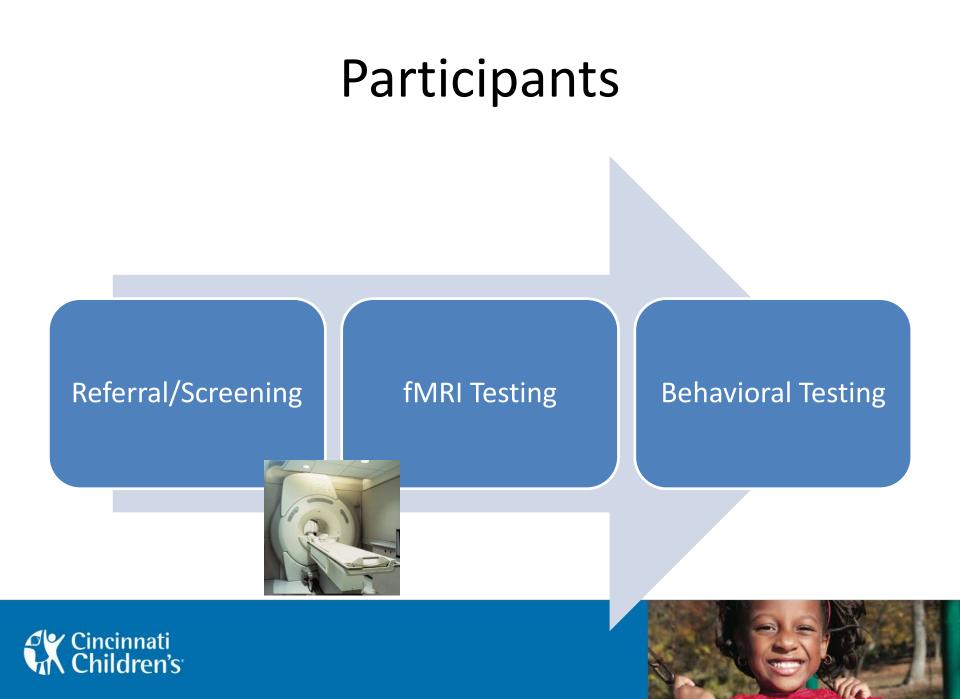


### Participants

- Inclusionary/exclusionary criteria
  - All participants:
    - No known co-occurring neurological disorder, genetic disorder, hearing loss, history of cleft, chronic medical condition that would impact speech or language
    - ADHD is not exclusionary
    - Right-handed
  - TSD: No diagnosed developmental disorder at any time history
  - SSD:
    - Language: Able to complete all scanning/testing activities







# Scanning

- Overview of methods with young children
  - Before the visit
    - Video
    - Practice
  - Pre-scan prep
    - Review behavioral tasks
    - Mock scanner
    - Quick tour of scanner room









### Scanning

#### • Entering the scanner

- SLOW process, parents in scan room has varying effectiveness
- Child "controls" the "spaceship" and "pilots" the spaceship with the buttons for raising and lowering the "Captain's Seat"
- Emergency button practice
- Sit on the scanner bed, sit next to them if needed
- Child tries the headphones on
- Child talks to an adult through the headphones the child talks back so that they know they can communicate
- Offer blanket, Children often don't know how to say or don't want to say that the temperature is uncomfortable

#### • During the scan

- Make sure that they can see the movie (the projector is on)
- Never ask the child if they are doing OK, tell them that they are doing a great job and ask if there is anything they want to tell us or if we can make them more comfortable
- If the child gets upset while in the scanner, have them go see their parent and they may be willing to go back in

Cincinnati Children's



# **Scanning Protocol**

- Total approximately 45-50 minutes
  - Anatomical scans (movie)
  - Functional scans (games)
    - Syllable repetition task (x2)(SRT)
    - Non-word imaging task (NIT)
    - Fine motor praxis task (FMPT)
  - Diffusion tensor imaging (movie)





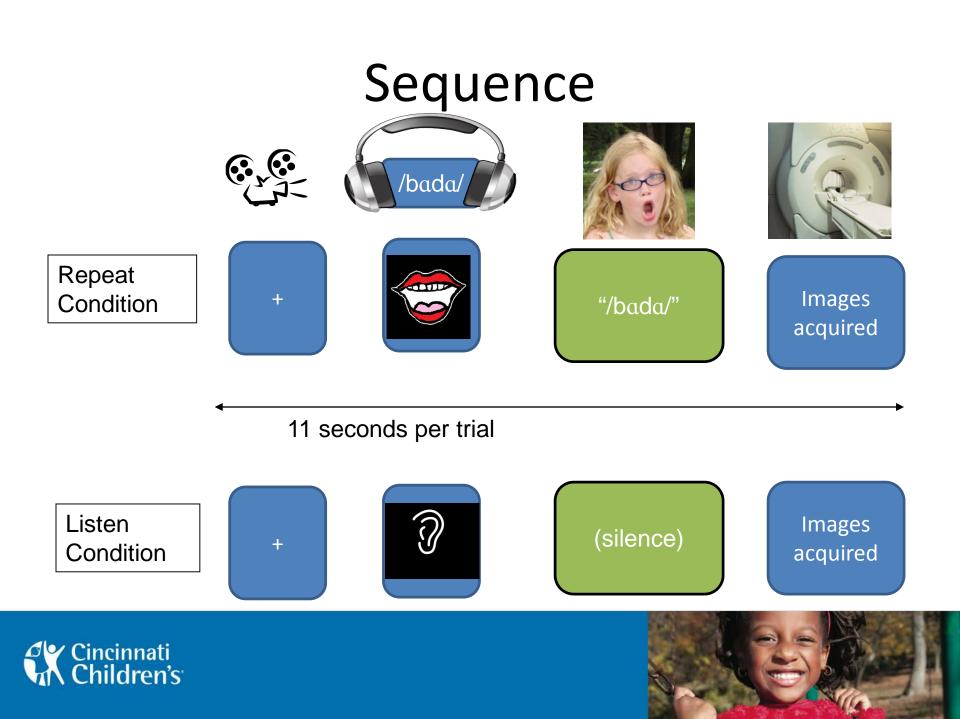
# Syllable Repetition Task

(Shriberg & Lohmeier , 2008; Shriberg et al., 2009; Lohmeier & Shriberg , 2011; Shriberg, Lohmeier, et al., 2012)

- During the SRT the child repeats phonetically simple phonemes (/b, d, m, n, a/) in syllables
  - Syllables increase in length from 2-4 syllables (e.g. /bada/ 'bada')
- Phonetically simple phonemes chosen to eliminate confounding elements of many non-word repetition tasks; easier phonemes support accurate production
- Attempts to minimize performance as an confounder
- 18 spoken items, 18 listen items, HUSH acquisition
- Active condition of repetition contrasted with listening
- Responses recorded and scored







# Fine Motor Praxis Task

- Novel task, developed to assess more complex finger tapping
- Hear sequence of 1-4 tones, bilaterally tap successive fingers to thumb matching the number of tones
- Contrasted with listening
- Total of 18 tapping trials, 18 listen trials
- Block acquisition





# SequenceImage: Second transformed by the second transformed by



Cincinnati Children's



Hands are

still

# **Behavioral Testing**

- Speech
  - Goldman Fristoe Test of Articluation-2 (GFTA-2) (Goldman & Fristoe, 2000)
  - Oral Speech Motor Screening Examination-3 (Louis & Ruscello, 2000)
  - Selected components of the Madison Speech Assessment Protocol, including a conversational analysis
- Language
  - Clinical Evaluation of Language Fundamental-4 (CELF-4) Core Test (Semel, Wiig, & Secord, 2003)
  - Comprehensive Test of Phonological Processing (CTOPP) (Wagner, Torgesen, & Rashotte, 1999)
  - Test of Auditory Processing Skills-3 (TAPS-3), Discrimination sub-test only (Martin & Brownell, 2005)
- Wechsler Abbreviated Test of Intelligence (WASI) (Wechsler, 2003)
- Purdue Pegboard
- School Function Assessment (SFA) (Coster, Deeney, Haltiwanger, & Haley, 1998)
- Parents complete a case history
- Hearing screening





# Summary of Participants

- Total of 27 children completed scanning
  - 11 TSD (7.7 years, range 6-10, males=7)
  - 16 SSD (7.1 years, range 5-9, males=11)
- Behavioral testing\*
  - 10 of 11 TSD completed
  - 15 of 16 SSD completed





### Speech and Language Testing Results for Children in the TSD and SSD Groups Compared Using Two-tailed t-Test (with Standard Deviations in Parentheses)\*

Test	TSD Mean (standard deviation)	SSD Mean (standard deviation)
GFTA Standard Score	104.8 (3.3)	78.3 (20.2)**
CELF Total Standard Score	103.0 (13.4)	79.6 (21.9)**
Concepts and Following Directions	12.3 (1.8)	8.1 (3.2)**
Word Structure	11.7 (2.3)	7.7 (4.2)*
Recalling Sentences	12.0 (2.8)	5.0 (2.8)**
Formulated Sentences	11.9 (3.0)	7.0 (4.4)**
Word Discrimination (TAPS) Standard Score	11.2 (2.0)	8.1 (2.5)**
СТОРР		
Phonological Awareness	103.4 (16.7)	83.2 (18.2)*
Phonological Memory	101.5 (7.5)	77.1 (13.9)**
Rapid Naming	98.2 (16.3)	87.3 (10.6)

\* *p* <.05, \*\* *p*<.01





Intelligence Testing Results for Children in the TSD and SSD Groups Compared Using Two-tailed t-Test (with Standard Deviations in Parentheses)\*

Test	TSD Mean (standard deviation)	SSD Mean (standard deviation)
Full IQ	109.1 (9.6)	97.4 (11.9)*
Verbal IQ	108.4 (14.6)	94.9 (10.0)*
Performance IQ	107.7 (11.4)	99.8 (14.0)

\* *p* <.05, \*\* *p*<.01





Fine Motor Dexterity and Functional Fine Motor Performance Test Results for Children in the TSD and SSD Groups Compared Using Two-tailed t-Test (with Standard Deviations in Parentheses)\*

Test	TSD Mean (standard deviation)	SSD Mean (standard deviation)
Purdue Pegboard Pin Test Right Hand	11.8 (1.5)	8.7 (1.8)**
Purdue Pegboard Pin Test Left Hand	10.1 (1.8)	7.8 (1.3)**
Purdue Pegboard Pin Test Combined	8.3 (1.7)	6.5 (1.8)*
School Function Total Assessment	36.3 (.5)	34.0 (2.8)
Using Materials	100.0 (0.0)	97.4 (4.2)
Clothing Management	68.0 (0.0)	62.5 (8.1)
Written Work	47.2 (1.3)	39.0 (8.0)*







SRT Results for Children in the TSD and SSD Groups During Scanning Compared Using Two-tailed t-Test (with Standard Deviations in Parentheses)\*

Test	TSD Mean (standard deviation)	SSD Mean (standard deviation)
SRT Run 1	12.5 (3.8)	10.2 (4.0)
SRT Run 2	12.8 (3.0)	8.5 (3.3)**
Total SRT	25.9 (5.9)	17.6 (7.0)**

\* *p* <.05, \*\* *p*<.01





# References

- Coster, W., Deeney, T., Haltiwanger, J., & Haley, S. (1998). *School Function Assessment*. San Antonio, TX: The Psychological Corporation.
- Goldman, R., & Fristoe, M. (2000). *Goldman-Fristoe Test of Articulation-Second Edition*. Circle Pines, MN: American Guidance Services, Inc.
- Lohmeier, H.L. & Shriberg, L.D. (2011). *Reference Data for the Syllable Repetition Task (SRT)* (Tech. Rep. No. 17). Phonology Project, Waisman Center, University of Wisconsin-Madison.
- Louis, K. O., & Ruscello, D. (2000). Oral Speech Mechanism Screening Examination- Third Edition. Dallas, TX: Pro-Ed.
- Shriberg, L.D. & Lohmeier, H.L. (2008). *The Syllable Repetition Task* (Tech. Rep. No. 14). Phonology Project, Waisman Center, University of Wisconsin-Madison.
- 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., Lohmeier, H.L., Strand, E.A., & Jakielski, K. J. (2012). Encoding, memory, and transcoding deficits in Childhood Apraxia of Speech. *Clinical Linguistics & Phonetics*, *26*, 445-482.
- Tkach, J.A., Chen, X., Freebairn, L.A., Schmithorst, V.J., Holland, S.K., & Lewis, B.A. (i2011). Neural Correlates of Phonological Processing in Speech Sound Disorder: A Functional Magnetic Resonance Imaging Study, *Brain and Language*. *119*,42-49.
- Vargha-Khadem, F. et al. (2005). FOXP2 and the Neuroanatomy of Speech and Language. *Nature (6)*, 131-138.
- Wechsler, D. (2003). WISC-IV: Wechsler Intelligence Scale for Children-Fourth Edition. San Antonio, TX: PsychCorp (Harcourt Assessment).





# Madison CAS Phenotype: Premises, Methods, and Classifications

Lawrence D. Shriberg Waisman Center University of Wisconsin-Madison

Neuroimaging of Children With Speech Sound Disorders American Speech-Language-Hearing Association National Convention, Atlanta, GA November 16, 2012

# Madison CAS Phenotype: Four Premises

### Premise 1 CAS is One of Three Subtypes of Motor Speech Disorders

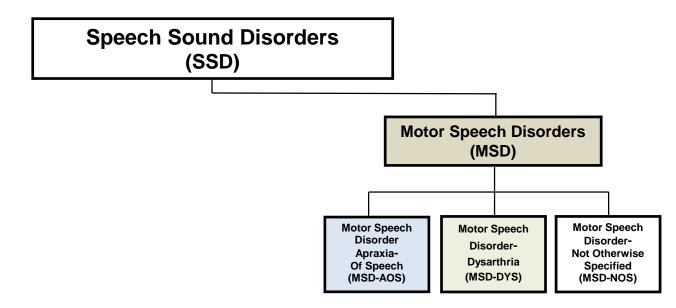
Childhood Apraxia of Speech (CAS) is one of three subtypes of a class of Speech Sound Disorders (SSD) termed Motor Speech Disorders (MSD)

Cover term: Speech Sound Disorders (SSD) Class term: Motor Speech Disorders (MSD)

Subtype terms:

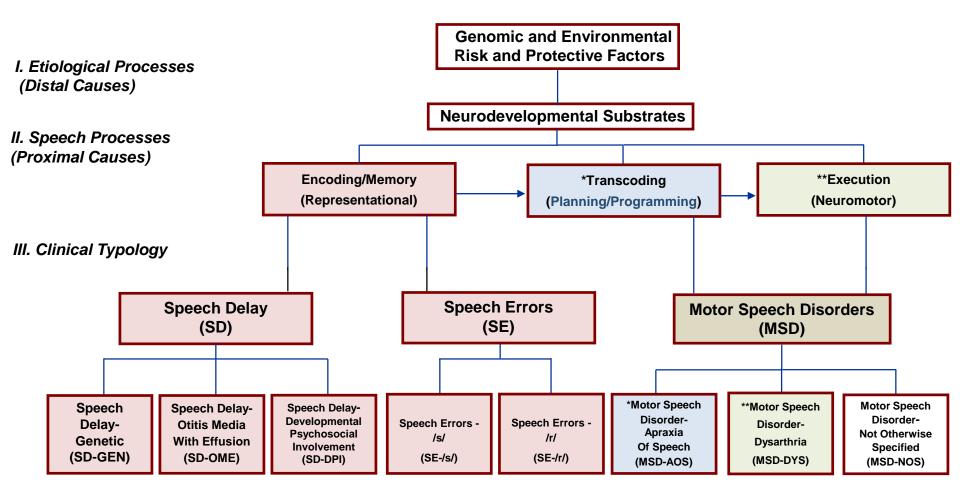
Motor Speech Disorder-Apraxia of Speech (MSD-AOS) Motor Speech Disorder-Dysarthria (MSD-DYS) Motor Speech Disorder-Not Otherwise Specified (MSD-NOS)

# **Premise 1** CAS is One of Three Subtypes of MSD



### Premise 2 A Transcoding Deficit Differentiates CAS from Speech Delay, MSD-DYS, and MSD-NOS

Speech Disorders Classification System (SDCS)



### **Premise 3:** Genetic and Behavioral Findings in CAS are Consistent With a Multiple Domain Disorder

### □ *FOXP2* – CAS Studies

- FOXP2 expression is bilateral and widespread, including gene regulation in pathways for vision, audition, speech, and other domains (e.g., Horng et al., 2009)
- Histories of cognitive, auditory-perceptual, language, motor, and psychosocial deficits (Rice et al., 2012; Shriberg et al., 2006; Tomblin et al., 2009)
- CAS Studies in Idiopathic, Neurogenetic, and Complex Neurodevelopmental Contexts
  - Histories of cognitive, auditory-perceptual, language, motor, and psychosocial deficits (Laffin et al. 2012; Raca et al., 2012; Shriberg, Lohmeier, et al., 2012; Worthey et al., 2012)

### Premise 4:

### Behavioral Markers of CAS Are Central to the Identification of Biomarkers and Theory

The inclusionary criteria (segmental and suprasegmental signs) that comprise the behavioral markers in studies of CAS will have significant impact on the success of two primary goals of next-generation CAS research

Identification of Biomarkers:

- Identification of biomarkers of CAS from neuroimaging and other methods
- □ Theory Confirmation:
  - Development and testing of alternative accounts of speech processing in CAS derived from emerging cognitive neuroscience frameworks (e.g., DIVA [Terband, Guenther, Maassen, others]; dual-stream models [Hickok, Poeppel, others])

# Madison CAS Phenotype: Methods

# Methods A Four-Sign Diagnostic Marker to Discriminate CAS from Speech Delay<sup>a</sup>

**Classification Criterion for CAS:** 

**Positive Finding on at least three of four signs of CAS** 

Sign	Finding	
Low Appropriate Pauses (AP)	+	
Low Articulatory Rate (AR)	+	
Low Appropriate Stress (AS)	+	
Low Accurate Transcoding (AT)	+	
	Any 3 or more = CAS	

<sup>a</sup> Shriberg, Strand, Jakielski, & Lohmeier (2012)

### **Methods**

# Three of the Four Diagnostic Signs Are Obtained from the MSAP Conversational Speech Sample

### Low Appropriate Pauses (AP)<sup>a</sup>

A 10-category pause typology and acoustic displays are used to derive the percentage of appropriate pauses Low Articulatory Rate (AR)<sup>a</sup>

The pause data and acoustic displays are used to derive an average articulation rate (syllables/second) Low Appropriate Stress (AS)

Codes from the Prosody-Voice Screening Profile (PVSP: Shriberg, Kwiatkowski, & Rasmussen, 1990) are used to derive the percentage of utterances without excessive-equal stress and other types of inappropriate stress

<sup>a</sup> Low (+) = z-score < 1 SD from the mean of a referent group of same age-gender typical speakers.

### **Methods**

# The Fourth Diagnostic Sign is Obtained from the Syllable Repetition Task (SRT)<sup>a</sup>

### Sign: Low Accurate Transcoding (AT)

- 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

<sup>a</sup> Shriberg & Lohmeier (2008); Shriberg et al. (2009); Lohmeier & Shriberg (2011); Shriberg, Lohmeier, et al. (2012)

# Methods Low Accurate Transcoding<sup>a</sup>

	Examples of Inaccurate Transcoding				
SRT <u>Item</u>	Homorganic Nasal	Heterorganic Nasal	<u>Non-Nasal</u>		
bada	ba <u>nd</u> a	ba <u>md</u> a			
mada			ma <u>rd</u> a		
nabada			naba <u>vd</u> a		
	AT Percentage = 1 -	No. of Addition	s X 100		
		No. of Eligible Stop Co			
	Low AT = < 80%				

<sup>a</sup> Addition of a nasal consonant was the most common addition (92%) in Shriberg, Lohmeier, et al. (2012)

# Madison CAS Phenotype: Classifications

### **Madison Speech Sound Disorders Classifications**

Participants	Age (yrs) Percentage of Consonants Correct (PCC)		3/4 Sign Diagnostic Marker (+ = Positive CAS Sign)			Total Number of Positive CAS Signs	
		Pausing	Rate	Stress	Transcoding		
CAS							
CIN02	8	54.5	+	+	+	+	4
CIN05	8	87.8	+	—	+	+	3
CIN06	10	88.0	+	+	+	+	4
CIN11	8	78.6	+	+	+	—	3
CIN22	6	77.1	+	+	+	+	4
Mean	8.0	77.2					3.6
Speech Delay							
or MSD-NOS							
CIN08	8	79.6	+	—	—	—	1
CIN10	8	86.1	+	—	—	+	2
CIN13	6	78.9	—	+	—	+	2
CIN14	8	68.5	+	—	—	—	1
CIN15	6	83.5	+	—	—	_	1
CIN20	8	92.1	+	_	—	+	2
Mean	7.3	81.5					1.5
Controls							
CIN03	8	93.4	+	—	—	—	1
CIN07	9	95.8	—	—	+	—	1
CIN09	8	93.9	—	—	—	—	0
CIN16	8	95.2	—	—	—	*a	0
CIN17	8	98.6	—	—	—	—	0
CIN18	7	89.5	+	+	_	_	2
CIN19	6	94.8	+	+	_	_	2
Mean	7.7	94.5					0.9

#### <sup>a</sup>SRT not administered

63.7% agreement with referral diagnosis

# References

- Horng, S., Kreiman, G., Ellsworth, C., Page, D., Blank, M., Millen, K., & Sur, M. (2009). Differential gene expression in the developing lateral geniculate nucleus and medial geniculate nucleus reveals novel roles for Zic4 and Foxp2 in visual and auditory pathway development. *The Journal of Neuroscience*, 29, 13672-13683.
- Laffin, J.J.S., Raca, G., Jackson, C.A., Strand, E.A., Jakielski, K.J., & Shriberg. L.D. (2012). Novel candidate genes and regions for Childhood Apraxia of Speech (CAS) identified by array comparative genomic hybridization. *Genetics in Medicine*. doi: 10.1038/gim.2012.72. [Epub ahead of print]
- Lohmeier, H.L. & Shriberg, L.D. (2011). *Reference Data for the Syllable Repetition Task (SRT)* (Tech. Rep. No. 17). Phonology Project, Waisman Center, University of Wisconsin-Madison.
- Raca, G., Baas, B.S., Kirmani, S., Laffin, J.J., Jackson, C.A., Strand, E.A., Jakielski, K.J., & Shriberg, L.D. (2012). Childhood Apraxia of Speech (CAS) in two youth with 16p11.2 microdeletion syndrome. *European Journal of Human Genetics*. doi: 10.1038/ejhg.2012.165. [Epub ahead of print].
- Rice, G.M., Raca, G., Jakielski, K.J., Laffin, J.J., Iyama-Kurtycz, C., Hartley, S.L. . . . Shriberg, L.D. (2012). Phenotype of *FOXP2* haploinsufficiency in a mother and son. *American Journal of Medical Genetics: Part A.* doi:10.1002/ajmg.a.34354 [Epub ahead of print].
- Shriberg, L.D., Ballard, K.J., Tomblin, J.B., Duffy, J.R., Odell, K.H., & Williams, C.A. (2006). Speech, prosody, and voice characteristics of a mother and daughter with a 7;13 translocation affecting *FOXP2*. *Journal of Speech, Language, and Hearing Research*, *49*, 500-525.
- Shriberg, L.D., Kwiatkowski, J., & Rasmussen, C. (1990). *The Prosody-Voice Screening Profile*. Tucson, AZ: Communication Skill Builders.
- Shriberg, L.D. & Lohmeier, H.L. (2008). *The Syllable Repetition Task* (Tech. Rep. No. 14). Phonology Project, Waisman Center, University of Wisconsin-Madison.
- 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.

# References

- Shriberg, L.D., Lohmeier, H.L., Strand, E.A., & Jakielski, K. J. (2012). Encoding, memory, and transcoding deficits in Childhood Apraxia of Speech. *Clinical Linguistics & Phonetics*, *2*6, 445-482.
- Shriberg, L.D., Strand, E.A., Jakielski, K.J., & Lohmeier, H.L. (2012). A diagnostic marker to discriminate Childhood Apraxia of Speech from Speech Delay. Manuscript submitted for publication.
- Tomblin, J.B., O'Brien, M., Shriberg, L.D., Williams, C., Murray, J., Patil, S., et al. (2009). Language features in a mother and daughter of a chromosome 7;13 translocation involving *FOXP2*. *Journal of Speech, Language, and Hearing Research*, *5*2, 1157-1174.
- Worthey, E., Dimmock, D., Raca, G., Laffin, J.J., Strand, E.A., Jakielski, K.J., & Shriberg, L.D. (2012). *Genetic heterogeneity and novel pathways in Childhood Apraxia of Speech (CAS) identified though whole exome sequencing*. Manuscript submitted for publication.

# **Preliminary Results**

**Neuroimaging of Children With Speech Sound Disorders** 

### American Speech-Language-Hearing Association National Convention, Atlanta, GA November 16, 2012

Jennifer Vannest, Ph.D. Assistant Professor, Division of Neurology Assistant Director, Pediatric Neuroimaging Research Consortium Cincinnati Children's Hospital Medical Center

jennifer.vannest@cchmc.org





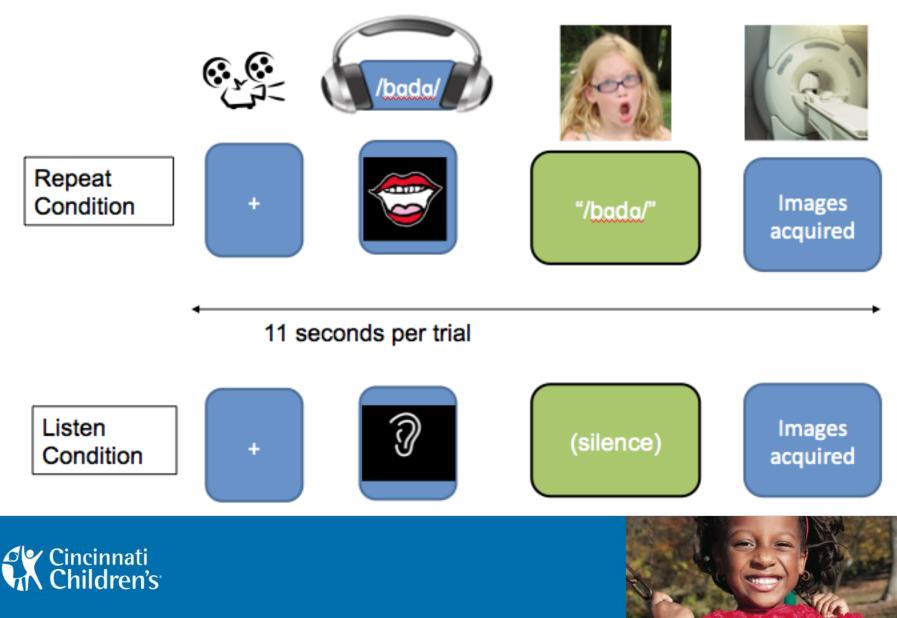
# fMRI Data Analysis

- Each fMRI data set was coregistered to correct for motion. Single volumes highly contaminated by motion were removed from analysis.
- Participants with less than 50% of volumes in each condition remaining were not included in further analysis
- Spatial normalization into Talairach space
- General linear model and paired t test were implemented to identify voxels activated by each task for each participant.
- Random- effects analysis was performed to determine significant group activations
- All results p<.05 corrected





# Syllable Repetition Task



# Syllable Repetition Task

- TSD n=6 (4F, mean age 8.0 years)
   SRT total score mean= 25.2
- SSD n=8 (2F, mean age 7.5 years)
   SRT total score mean= 19.6
- Madison Protocol
  - -4 SD
  - 2 Insufficient data, 1 to-be-analyzed
  - -1 CAS





### Speech and Language Testing Results for TSD and SSD Children Included in the SRT Analysis Using Two-tailed t-Test (with Standard Deviations in Parentheses)\*

Test	TSD Mean (standard deviation)	SSD Mean (standard deviation)
GFTA Standard Score	102.8 (2.9)	77.0 (19.1)**
CELF Total Standard Score	103.8 (18.0)	82.7 (22.8)
Concepts and Following Directions	12.3 (2.2)	8.5 (4.7)
Word Structure	11.8 (3.2)	7.7 (4.2)*
Recalling Sentences	12.2 (3.9)	5.6 (3.4)*
Formulated Sentences	12.0 (2.5)	7.6 (4.7)*
Word Discrimination (TAPS) Standard Score	11.4 (2.6)	8.1 (2.6)*
СТОРР		
Phonological Awareness	113.8 (12.1)	86.0 (23.1)*
Phonological Memory	104.5 (1.7)	76.0 (18.2)*
Rapid Naming	103.8 (19.4)	85.3 (6.4)

\* *p* <.05, \*\* *p*<.01





Intelligence Testing Results for TSD and SSD Children Included in the SRT Analysis Using Two-tailed t-Test (with Standard Deviations in Parentheses)\*

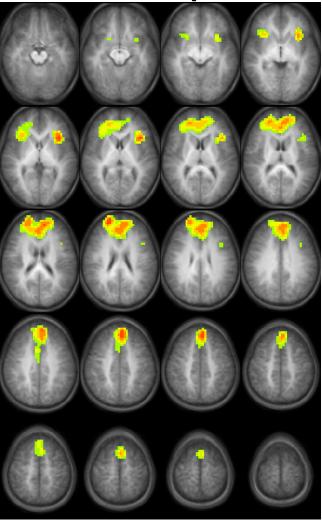
Test	TSD Mean (standard deviation)	SSD Mean (standard deviation)
Full IQ	110. (13.2)	94.2 (13.1)
Verbal IQ	104.5 (15.7)	100.2 (15.7)
Performance IQ	108.3 (11.5)	97.7 (14.9)

\* *p* <.05, \*\* *p*<.01

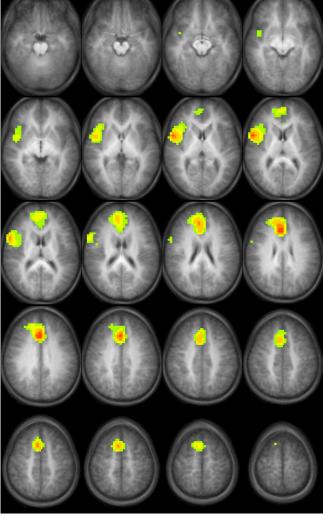




# Syllable Repetition Task: Repeat>Listen



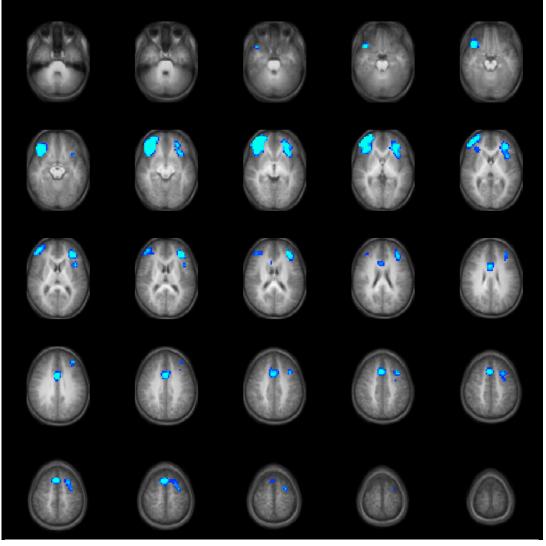
TSD







### Syllable Repetition Task: Regression with task performance



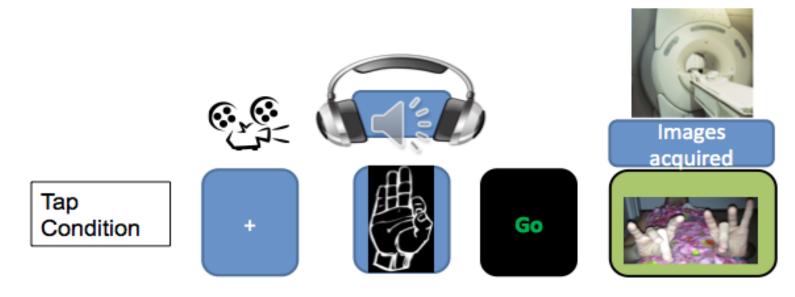
Higher SRT score  $\rightarrow$  lower level of activation





R

# Fine Motor Praxis Task





Cincinnati Children's



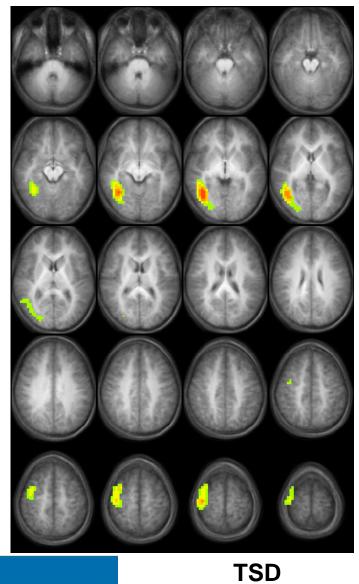
# Fine Motor Praxis Task

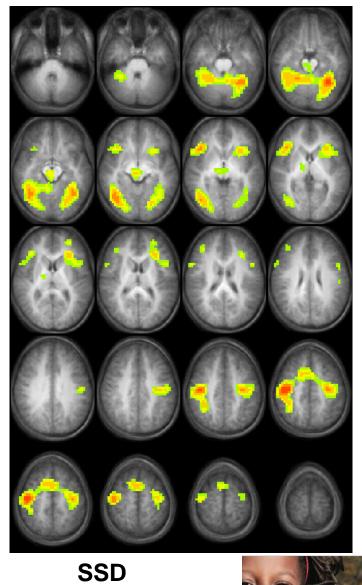
- Age-matched groups (n=12)
  TSD n=6 (8.3 years, 3 males)
  SSD n=6 (8.0 years, 3 males)
- For this limited group, no significant differences in SFA scores or IQ scores
- Purdue Pegboard Scores significantly different for right hand (p=.001) but not for left hand and combined
- Madison Protocol
  - 3 SD
  - 2 Insufficient data
  - 1 CAS

Cincinnati Children's



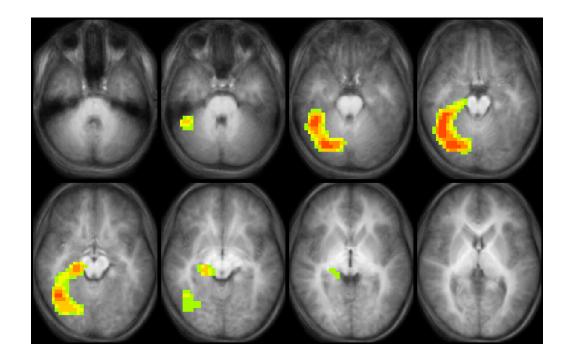
### Fine Motor Praxis Task: Tap>Listen





Cincinnati Children's

# Fine Motor Praxis Task: SSD>Controls









L

# Summary

- Children with SSD have similar activation of speech motor networks to TSD children during a speech production task
  - o slightly more right-lateralized pattern in SSD
- Level of activation is highly tied to task performance across groups: less activation associated with better performance





# Summary

- Children with SSD have higher levels of activation than TSD during a manual fine motor praxis task
- Regions of maximum difference between groups were in R parahippocampal and fusiform gyrus
   Associated with long-term memory and recognition of familiar objects i.e. body parts
- Additional data will be needed to potentially differentiate subtypes of SSD



