Apraxia of Speech and Nonverbal School-Aged Children with Autism

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Nonverbal School-aged Children with Autism
NIH Workshop, Bethesda, MD, April 13-14, 2010

Topics

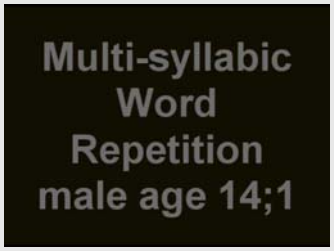
I. Introduction
   A. Apraxia of Speech
   B. The CAS/ASD Hypothesis
II. Overviews
   A. Speech Sound Disorders (SSD)
   B. Childhood Apraxia of Speech (CAS)
III. Speech Research in ASD
   A. Verbal ASD: Findings
   B. Nonverbal ASD: Perspectives

Locus of Apraxia of Speech in a Four-Phase Speech Processing Framework[a]

Encoding (auditory-perceptual)
↓
Memorial (storage, retrieval)
↓
Transcoding (planning-programming)
↓
Execution (neuromotor)

[a]After Van der Merwe (2009)

Apraxia of Speech in an Adolescent with Classic Galactosemia



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

What is Apraxia of Speech?

Say the following as quickly as you can:

Six thick thistle sticks
Six thick thistle sticks
Six thick thistle sticks

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The CAS/ASD Hypothesis[a]

CAS is a sufficient cause for:

Weak version: speech and prosody-voice deficits in persons with verbal ASD

Strong version: failure to acquire speech in persons with nonverbal ASD

[a]Childhood Apraxia of Speech (CAS) is the term adopted in the ASHA (2007) report; Developmental Verbal Dyspraxia (DVD) continues to be used in medical literatures and in most other countries

Motivation for the CAS/ASD Hypothesis

- Persons with ASD reportedly have praxic movement disorders (see elsewhere this workshop), implicating planning/programming deficits, the presumed speech processing locus of CAS
  - Speech acquisition and performance researchers argue from a number of perspectives that speech is domain specific (e.g., Kent, 2000, 2004, 2010; McCauley et al., 2009; Potter et al., 2009; Weismer, 2006; Ziegler, 2002, 2008)
- Persons with ASD reportedly have imitative deficits (see elsewhere this workshop), with implications for motor processes in speech acquisition
  - Imitation deficits are not a core speech-processing feature of CAS in frameworks such as in the widely accepted van der Merwe framework (2009); see also Kappes et al. (2009) and Terband and Maassen (2010)

Motivation for the CAS/ASD Hypothesis

- Persons with ASD reportedly have significantly reduced early nonverbal oral behaviors presumed to share neural substrates with speech and reported to predict speech fluency (Gernsbacher et al., 2008; Iverson & Wozniak, 2007; Page & Boucher, 1998; Seal & Bonvillion, 1997; see elsewhere this workshop)
- CAS is the only subtype of speech disorder in which the onset of speech (compared to speech precision or stability) is delayed (Shriberg, 2010a; however, see IIA)
- CAS and ASD were both implicated in recent genomic findings linking *FOXP2* to *CNTNAP2* (Poot et al., 2010; Vernes et al., 2008); CAS and ASD overlaps also reported for other candidate genes and regions of interest

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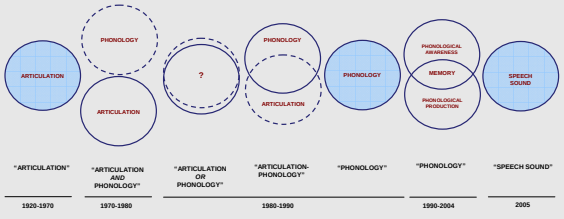
History of Classification Terms for SSD of Known and Idiopathic Origins



Eight Putative Etiological Subtypes of SSD of Currently Unknown Origin

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

Genomic Research in Speech Delay

- There have been no genes identified to date that code specifically for Speech Delay
- Several candidate genes for Speech Delay have been associated with language impairment and dyslexia, including regions of interest reported on 5 of the 22 autosomes: 1, 3, 6, 15, 16

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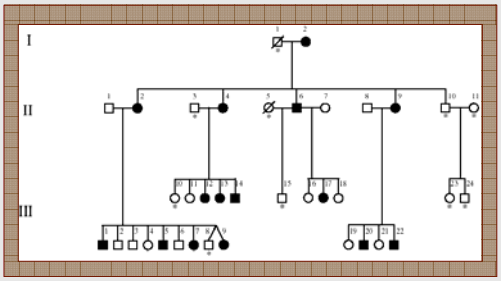
Research in CAS

- Genomic
- Phenotype
- Neuroimaging
  - e.g., Lewis (2008); Robin (2008)
- Speech Motor Control and Computational Neural Modeling;
  - e.g., Maas, Robin, Wright, et al. (2008); Terband et al. (2009); Terband and Maassen (2010); Wright et al. (2009)
- Treatment
  e.g., Maas, Robin, Austermann Hula, et al. (2008)

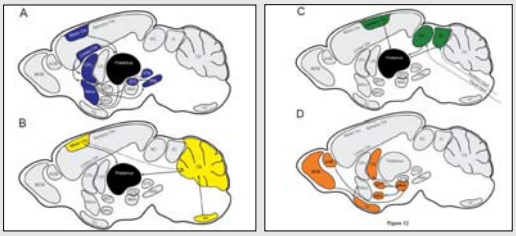
Genomic Research in CAS: The Iconic Pedigree



Genomic Research in CAS: Some *FOXP2* Highlights

- Molecular genetic and neurocognitive publications on the London 'KE' family beginning with Hurst et al. (1990) catalyzed worldwide interest from many disciplines in the possibility of speech-language genes
- Lai et al. (2001) identified *FOXP2* as the gene segregating in affected members of the family
- *FOXP2* disruptions and motor speech disorder consistent with CAS reported in four other families (MacDermot et al., 2005; Shriberg et al., 2006; Shriberg, 2010b; Zeesman et al., 2006)
- Continuing functional analyses of *FOXP2;* knockout, knockdown, and knockin Foxp2 orthologs in vertebrate species including rodents, birds, reptiles, and fish
- Zebra finch genome sequenced; parrot genome next

Alternative Neural Circuit Proposals for Foxp2 Expression in Mouse Vocalizations[a]



[a]Campbell et al. (2009)

Genomic Research in CAS: Madison Group

- CAS documented in three siblings with an unbalanced chromosome 4q;16q translocation (Shriberg, Jakielski, & El-Shanti, 2008)
- Phenotype studies of a mother and son in a new family with a *FOXP2* disruption, including possible ASD in the son
- Array Comparative Genomic Hybridization (aCGH; copy number) studies of children with idiopathic CAS
- Resequencing studies of five children with idiopathic CAS; exome analyses covering > 90% of the protein coding subset of the genome

Phenotype Research in CAS

- "…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)

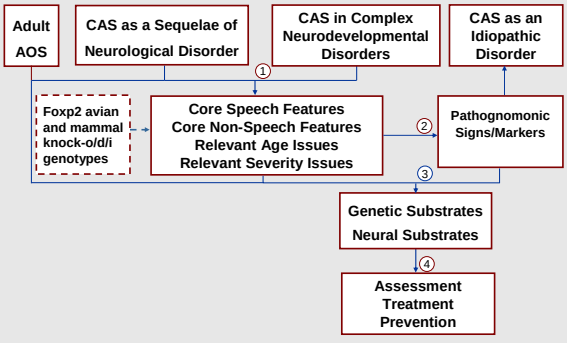
Phenotype Research in CAS: The Phenotype Constraint

- No biomarker for CAS
- No one behavioral marker pathognomonic for CAS
- No set of behavioral markers with high diagnostic accuracy for CAS

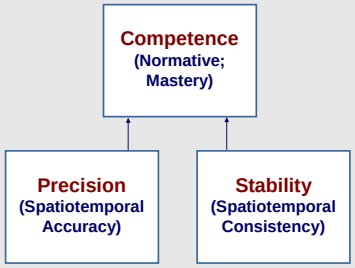
Phenotype Research in CAS: Phenotype Constraints in *FOXP2* Studies

- Clinical assessment of affected KE family members not reported to date. The measures identifying affected from unaffected KE family members were speech services, and performances on non-standardized nonsense word repetition tasks and oral motor tasks.
- Speech data from KE family and from family members in two other *FOXP2* families are consistent with dysarthria, as well as apraxia of speech (Morgan et al., 2005; Shriberg, 2010b; Shriberg et al., 2006).
- *FOXP2* has low attributable risk for CAS.

CAS Research: Madison Phenotype Research



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



[a]Shriberg, Fourakis, et al. (2010)

Complex Neurodevelopmental Disorders Reporting 'Significant Speech Delay'/CAS

- Autism
- Chromosome Translocations
- Down syndrome (Trisomy 21)
- Rolandic Epilepsy
- Fragile X syndrome (*FMR1*)
- Joubert syndrome (*CEP290*; *AHI1*)
- Galactosemia
- Rett syndrome (*MeCP2*)
- Russell-Silver syndrome (*FOXP2*)
- Velocardiofacial syndrome (22q11.2 deletion)

Identifying Markers of CAS in Neurogenetic Contexts Can Inform Markers of Idiopathic CAS

- Findings to date are interpreted as support for the premise that an operationalized and standardized set of perceptual and acoustic markers of CAS can be identified from and cross validated in participants with CAS in complex neurogenetic disorders.
- Promising markers identified to date in three domains of speech production – vowels, rate, stress – are consistent with the spatial and timing consequences of deficits in transcoding (planning/programming) processes.

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Speech and Prosody-Voice Studies in Children with Verbal ASD

- Fewer than one dozen, methodologically 'adequate' descriptive-explanatory studies
- Few speech studies have included dependent variables assessing prosody and voice
- Few studies have used quantitative metrics from motor speech, rather than phonological literatures
- Few studies have augmented auditory-perceptual methods (broad or narrow phonetic transcription) with instrumental methods (e.g., acoustics, kinematics)

Speech and Prosody-Voice Findings in Verbal ASD

Speech Delay (SD)

- Children with verbal ASD are at higher risk for Speech Delay
  - Estimated population prevalence of SD:
    3 years: 15.2% - Campbell et al. (2003); Shriberg et al. (1999)
    6 years: 3.8% - Campbell et al. (2003); Shriberg et al. (1999)
  - Estimated prevalence of SD in verbal ASD:
    4-5 years (*n*=24): 15% - Shriberg, Paul, et al. (2010)
    6-7 years (*n*=22): 9% - Shriberg, Paul, et al. (2010)
    5-13 years (*n*=69): 12% - Cleland et al. (2010)
    $\bar{X}$: 8.5 years (*n*=62): 24% - Rapin et al. (2009)

Speech and Prosody-Voice Findings in Verbal ASD

Speech Errors (SE)

- Adolescents and adults with verbal ASD reported to have >10-fold population risk for Speech Errors
  - Estimated population prevalence of SE:
    2-3% - Flipsen (1999)
  - Estimated prevalence of SE in verbal ASD:
    30% - Shriberg, Paul, et al. (2001)
    33% - Cleland et al. (2010)

Speech and Prosody-Voice Findings in Verbal ASD

Motor Speech Disorder (MSD)

Velleman et al. (2010)

- Ten 4 to 6.5 year-old children with verbal ASD
- Extensive assessment protocol
- Perceptual and acoustic methods

- Frank CAS not observed in any of the participants
- No support for dysarthria
- Atypical values for many children on indices reported in studies of adults with motor speech disorders could be interpreted as support for MSD-NOS

The Hypothesis of Apraxia of Speech in Children with Autism Spectrum Disorder[a]

- 46 participants (72% male) with verbal ASD;
  > 70% intelligibility an inclusionary criterion
- 10-14 participants at each age from 4-7 years
- Conversational speech sample from ADOS
  - Narrow phonetic transcription
  - Prosody-voice coding
  - Acoustic analyses
- Competence, Precision, Stability Analytics (CPSA) in PEPPER environment

[a]Shriberg, Paul, and colleagues (2010)

Findings Do Not Support the CAS/ASD Hypothesis in Verbal ASD

Double dissociation:

- Compared to typical speakers and speakers with significant SD, young children with verbal ASD
  - do not have two of the three core signs of CAS reported in Shriberg (2010b): vowel errors and slow rate
  - do have a variant of the third sign, inappropriate prosody, but their unstable loudness, unstable fundamental frequency, and inappropriate stress is consistent with deficits in affective, pragmatic, and syntactic processes, not praxis speech processes (e.g., McCann & Peppe, 2003; Paul et al., 2005, 2008; Diehl et al., 2008; see Russo et al., 2008)

Topics

NIH Workshop Questions

1. What do we know about the CAS/ASD hypothesis?
2. What are the challenging research needs for the CAS/ASD hypothesis?
3. How might CAS be assessed in nonverbal ASD?

What do we know about the CAS/ASD hypothesis?

- No support for the strong version of the CAS/ASD hypothesis (i.e., for CAS in nonverbal ASD)
- Equivocal support for the weak version of the CAS/ASD hypothesis (i.e., for CAS in persons with verbal ASD)
- Some support for an alternative hypothesis—MSD-NOS in some persons with ASD

What do we know about the CAS/ASD hypothesis?

Some Counter-Support Perspectives

- Lack of support for the assumption of common neuromotor substrates for nonspeech and speech movements — a critical assumption linking findings of sensorimotor and imitation constraints in ASD to CAS.
- Lack of support from case reports of recovered nonverbal ASD. Such cases (Pickett et al., 2009) apparently do not have what should be perceptually salient speech, prosody, and voice features consistent with CAS, minimally to include persistent vowel distortions, slow rate, and inappropriate lexical and sentential stress.
- Lack of cognitive intent would seem to be a sufficient explanation for nonverbal ASD, particularly when supported by evidence of failure to acquire other forms of communication. Support for the CAS/ASD hypothesis would require evidence for CAS in such participants

What are the challenging research needs for the CAS/ASD hypothesis?

- Need a biomarker of CAS, a pathognomic behavioral marker of CAS, or a set of behavioral markers of CAS—the latter two based on minimal vocalizations
- Need a thorough database of the repertoires of persons with nonverbal ASD and communicative intent, using perceptual and instrumental methods (e.g., Sheinkopf et al. (2000)
  - Vowel and consonant systems, prosodic repertoires, and laryngeal and resonance values in diverse environmental and interlocutor contexts.

What are the challenging research needs for the CAS/ASD hypothesis?

- Genomic, neuroimaging, and behavioral studies of nonverbal and verbal ASD, toward identifying their neurocognitive and neuromotor substrates
- Treatment studies operationalizing the relevant substrates to demonstrate proof of principle
- Animal models of vocal development informed by genomic findings, to develop targeted pharmacogenomic prevention and treatment

How might CAS be assessed in nonverbal ASD?

- Analyses of speech and prosodic repertoires obtained from natural and structured protocols
- Analyses of the repertoires obtained from dynamic (rather than static) assessment
  - Strand et al. (2010) report promising validity and reliability for a dynamic assessment task
- Analyses of response to static and dynamic assessment protocols evoked using emerging technologies (e.g., computer media, robotic agents)

Thanks . . .

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

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