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Prevalence and Phenotype of Childhood Apraxia of Speech in Youth With Galactosemia

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Purpose: In this article, the authors address the hypothesis that the severe and persistent speech disorder reported in persons with galactosemia meets contemporary diagnostic criteria for Childhood Apraxia of Speech (CAS). A positive finding for CAS in this rare metabolic disorder has the potential to impact treatment of persons with galactosemia and inform explanatory perspectives on CAS in neurological, neurodevelopmental, and idiopathic contexts.
Method: Thirty-three youth with galactosemia and significant prior or persistent speech sound disorder were assessed in their homes in 17 states. Participants completed a protocol yielding information on their cognitive, structural, sensorimotor, language, speech, prosody, and voice status and function.
Results: Eight of the 33 participants (24%) met contemporary diagnostic criteria for CAS. Two participants, 1 of whom was among the 8 with CAS, met criteria for ataxic or hyperkinetic dysarthria. Groupwise findings for the remaining 24 participants are consistent with a classification category termed *Motor Speech Disorder–Not Otherwise Specified* (Shriberg, Fourakis et al., 2010a).
Conclusion: The authors estimate the prevalence of CAS in galactosemia at 18 per hundred—180 times the estimated risk for idiopathic CAS. Findings support the need to study risk factors for the high occurrence of motor speech disorders in galactosemia despite early compliant dietary management.

Key Words: apraxia, dyspraxia, genetics, motor speech disorder, speech sound disorder

Consistent trends in the sparse literature on galactosemia and communicative disorders indicate high occurrence of significant and persistent speech sound disorder (SSD) in persons with galactosemia, with most reported speech findings consistent with developmental verbal dyspraxia. As recommended by the American Speech-Language-Hearing Association (ASHA, 2007), we hereafter reference apraxia of speech in children as *Childhood Apraxia of Speech* (CAS). The following three sections, respectively, review cognitive, language, and speech findings in galactosemia; summarize contemporary research issues in CAS; and describe rationale for the three questions about galactosemia and CAS addressed in this study.

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Galactosemia

Description

Galactosemia is an autosomal recessive metabolic disorder estimated to occur in 1 in 53,000 infants in the United States (National Newborn Screening and Genetics Resource Center; see http://nnsis.uthscsa.edu/xreports.aspx?XREPORTID=84&FORMID=102&FCLR=1). *Galactose* is one of two sugars that make up the complex milk sugar known as *lactose*. Individuals with galactosemia lack or have insufficient amounts of the galactose-1-phosphate uridylyltransferase enzyme needed to break down galactose, resulting in a toxic buildup of galactose-1-phosphate in the red blood cells. The most common genotype for galactosemia, Q188R/Q188R, was found in 62% of 107 cases of galactosemia described in Elsas, Langley, Paulk, Hjelm, and Dembure (1995). Individuals who are homozygous for galactosemia have the Q188R allele on both of their ninth chromosomes in the 9q13 region, whereas other persons with galactosemia have different alleles, one of which may be a Q188R. The letters *Q* and

R are symbols for the amino acids glutamine (Q) and arginine (R). *Q188R* indicates that this allele results in a replacement of arginine for glutamine at position 188 in the galactosemia (GALT) protein. Significant cognitive, language, and speech disorders have been reported for all genotypes conferring risk for galactosemia, with homozygous Q188R associated with the largest risk for cognitive and verbal trait deficits (Elsas et al., 1995; Powell et al., 2009; Webb, Singh, Kennedy, & Elsas, 2003).

Infants in the United States and many European countries are tested for galactosemia in newborn screening programs by means of a heelstick blood sample. Because there is no requirement for the timeliness of notification, there is often a delay in providing screening results to doctors and parents. Within days of the initiation of milk feeding, infants with galactosemia develop jaundice and have liver and kidney dysfunction. The treatment for galactosemia is to immediately restrict from the diet all foods containing more than trace amounts of galactose, including human, cow, and goat milk. If infants are left untreated, the second week of life may include the development of cerebral edema, coagulopathy, muscle hypotonia, and E. coli septicemia, followed by death (Ridel, Leslie, & Gilbert, 2005). Of 53 reported births of infants with galactosemia in the United States in 2000, 35 (66%) had treatment initiated in the first week of life, 10 (19%) had treatment initiated in the second week of life, and 8 (15%) had treatment initiated in the third week of life or later (http://genes-r-us.uthscsa.edu/resources/newborn/00/ch5_complete.pdf). Botkin (2005) estimated that prior to newborn screening, 20%–30% of infants with galactosemia died. Newborn screening has reduced mortality from 33% to 15% in Ireland. Mortality statistics for galactosemia in the United States are not available.

Cognitive and Language Findings

Even with early initiation of a lactose-restricted diet, approximately 45% of children with galactosemia have IQs below standard scores of 85, and it has been estimated that approximately 52% have language impairments (Nelson, Waggoner, Donnell, Tuerck, & Buist, 1991; Waggoner, Buist, & Donnell, 1990). In a study of the same sample of 33 children with galactosemia and speech disorder to be described in the present report, 15 of the 17 (88%) participants with borderline-low cognition had receptive and expressive language impairment, and nine of the 16 (56%) participants with typical cognition had language impairment, most often affecting only expressive language (Potter, Lazarus, Johnson, Steiner, & Shriberg, 2008). It is crucial to note that, as found in a sample of 350 persons with galactosemia reported by Waggoner et al. (1990), the presence and severity of cognitive and language disorders in the sample of individuals whose speech characteristics are described in the present article were not associated with the duration of exposure to dietary lactose (Potter et al., 2008).

More recently, in a study using a birth order design, Hughes et al. (2009) reported cognitive-speech-language findings for the first child in the family diagnosed with galactosemia compared with outcomes for all the later-born children who have this autosomal recessive disorder. Whereas a lactose-restricted diet was initiated on or before 7 days after birth of the first sibling diagnosed with galactosemia, the younger siblings had essentially 0 days of exposure to lactose. Hughes et al. reported that maternal lactose restriction during pregnancy did not determine severity of cognitive-speech-language outcomes. The most neurologically affected participant in the Hughes et al. study was a later-born child whose mother had restricted her lactose intake throughout pregnancy. Toxic effects of lactose likely occurred during prenatal development due to the endogenous production of galactose. Waggoner and colleagues (1990) also reported that maternal lactose restriction during pregnancy did not appear to affect outcome severity.

Speech Findings

Table 1 is a summary of findings from a literature search on the speech of persons with galactosemia. The validity and reliability of lifetime estimates of the prevalence of CAS in galactosemia is constrained by the notable lack of consensus on the speech and other features that are sensitive to and specific for CAS. As shown in Table 1, speech assessment methods ranged from parent questionnaire information to the use of measures with limited sensitivity to and specificity for pediatric motor speech disorders. This limitation is shared by all reports of CAS in idiopathic and other contexts because, as discussed later, currently there is no validated standardized protocol and validated classification criteria to identify a speaker as true positive for CAS (ASHA, 2007; McCauley & Strand, 2008).

In a sample of 243 persons with galactosemia assessed by questionnaire more than 2 decades ago, the lifetime prevalence of speech disorders in persons with galactosemia was estimated at approximately 60% (Waggoner et al., 1990). In a subsample of 13 of the Waggoner et al. study participants who were evaluated by an in-person speech assessment, eight were diagnosed with apraxia of speech (AOS). An additional five of 11 children who were evaluated by telephone assessment were diagnosed with apraxia of speech (Nelson et al., 1991; Waggoner et al., 1990). The most widely cited speech finding from these and other studies is that approximately 55% (or one of every two children with galactosemia) meet clinical criteria for apraxia of speech (Nelson et al., 1991; Robertson, Singh, Guerrero, Hundley, & Elsas, 2000; Webb et al., 2003). Hughes and colleagues (2009) reported that 77% of

Table 1. Speech findings in 13 studies of persons with galactosemia.

Study		Participants		Speech assessment instrument	Speech findings (% participants)		
Year	Author(s)	*n*	Age(s) in years;months		AOS	Dysarthria	Speech disorder
1972	Lee	60	2;2–17;7	—	—	—	25%
1973	Jan & Wilson	1	19 yrs	—	—	100%	—
1983	Waisbren et al.	8	4;4–11;7	Variety of tests	—	—	63%
1990	Waggoner et al.[a]	243	2 wks–37 yrs	Questionnaire	56%	—	—
1991	Nelson et al.[b]	24	3;1–23;7	Local protocol	54%	—	8%
1992	Koch et al.[c]	2	24;0, 27;0	—	—	100%	—
1993	Waggoner & Buist[b]	163	—	Questionnaire	59%	—	—
1993	Schweitzer et al.	66	0;9–33;0	Denver Developmental Screener	14%	—	51%
1995	Sommer et al.	5	9 mos–27 yrs	—	—	—	20%
1996	Hansen et al.	8	0;9–19;2	ITPA	50% (3/6)	—	—
2000	Robertson et al.[d]	134	3–41 years	Apraxia Profile or questionnaire[g]	38%	—	—
2003	Webb et al.[e]	24	2;6–30	Apraxia Profile[g]	63%	—	—
2009	Hughes et al.[f]	26	—	—	—	—	77%[f]

Note. Em dashes indicate no available information. AOS = apraxia of speech; ITPA = Illinois Test of Psycholinguistic Abilities (Kirk et al., 1968).

[a]Diagnostic classifications for 24 of 243 participants by D. Nelson; 11 assessed in person and 13 assessed by telephone. [b]The same participants are also included in Waggoner et al. (1990). [c]The same siblings are described in Lo et al. (1984). [d]21 participants were assessed in person and 113 were assessed by questionnaire using retrospective data: 39% of the participants with Q188R/Q188R genotype, 38% with Q188R/Other genotype, and 36% with Other/Other genotype had apraxia. [e]The 21 participants assessed were the same participants as those reported in Robertson et al. (2000). [f]Authors indicated that of 26 participants tested, 77% "exhibited evidence of speech and language problems, predominantly verbal dyspraxia" (p. 723). [g]See Hickman (1997).

26 siblings with galactosemia "exhibited evidence of speech and language problems, predominantly verbal dyspraxia" (p. 723). Each of these prevalence estimates far exceeds a population prevalence estimate for idiopathic CAS of one per 1,000 children, a preliminary estimate extrapolated from clinical referrals to one university speech clinic (Shriberg, 2010a; Shriberg, Aram, & Kwiatkowski, 1997a; Shriberg & Kwiatkowski, 1994).

CAS

A Neurodevelopmental Research Framework for CAS

As noted previously, the primary methodological constraint in CAS research continues to be the lack of a standardized assessment procedure and inclusionary criteria that can be used to identify and classify a child as positive for CAS (ASHA, 2007; McCauley & Strand, 2008). Since the initial influential descriptions of AOS in children by Morley, Court, Miller, and Garside (1955), Rosenbek and Wertz (1972), and Yoss and Darley (1974), virtually every research report on CAS includes a caveat about measurement methods and inclusionary criteria in the interpretation of and generalizations from study findings. Contemporary discussions conclude that there is no consensus on the pathophysiology of CAS and, therefore, no consensus on the methods and classification criteria for identifying persons who are true positive for CAS (ASHA, 2007; Shriberg & Campbell, 2003). However, there is emerging consensus on the signs of acquired AOS (for rationale and extended literature reviews, see Duffy [2005] and Robin, Jacks, & Ramage [2008]), with researchers in CAS taking different positions on which of these signs are also necessary and sufficient for diagnostic classification of CAS (ASHA, 2007).

A recent literature review includes a proposal to address the inclusionary criteria problems in CAS research by studying CAS as it occurs in neurological, neurodevelopmental, and idiopathic contexts in children and adults (Shriberg, 2010b). The review includes a synthesis of findings from 18 studies reporting 55 cases of severe speech disorders consistent with CAS in the context of diverse complex neurodevelopmental disorders. In addition to speech deficits consistent with CAS, most cases had deficits in cognition and language, and many also had dysmorphologies and dysarthria. Such findings, by definition, contrast with studies of idiopathic CAS, in which candidate participants are typically excluded if they have frank cognitive deficits, dysarthria, or dysmorphologies. A central premise in Shriberg (2010b) is that compared with studies of CAS in idiopathic contexts, studies of participants with CAS in similar neurological or neurodevelopmental contexts reduces heterogeneity in causal pathways.

CAS in Neurodevelopmental Contexts

The most widely cited example of CAS in a complex neurodevelopmental context is the identification and continuing functional analyses of a point mutation in the *FOXP2* gene (chromosome 7q31) segregating with a severe and persistent SSD in approximately half the members of an extended family (Lai, Fisher, Hurst, Vargha-Khadem, & Monaco, 2001) and replicated, to date, in several other families (Feuk et al., 2006; MacDermot et al., 2005; Rice et al., 2011; Shriberg et al., 2006; Shriberg, Jakielski, et al., 2011; Zeesman et al., 2006). A substantial body of evidence also demonstrates that deficits in *Foxp2* (orthologs of *FOXP2* are indicated in lower case) in other vertebrate species are sufficient to disrupt both unlearned and learned vocal behaviors (see comprehensive reviews in Fisher & Marcus, 2006; Ramus & Fisher, 2009). It is important to note, however, that for the present focus on CAS as a pediatric SSD, several unpublished studies in North America have failed to find *FOXP2* disruptions in moderately large samples of children reported to have CAS, suggesting that hereditary or de novo *FOXP2* disruptions do not account for a significant proportion of persons meeting varying diagnostic classification criteria for CAS.

Other regions of interest and candidate genes for CAS have been reported. Shriberg, Jakielski, and El-Shanti (2008) described genetic, morphologic, and speech findings for three siblings with a similar unbalanced chromosome 4q;16q translocation. The children, each of whom was monosomic for a telomeric region on chromosome 4 that contains 11 genes, have been treated for CAS for many years. Three of the annotated genes on chromosome 4 have no known function in humans, raising the question of their possible role in speech processing. Lewis (2008) described genetic, neuroimaging, and speech findings for a child with severe and persistent SSD associated with a disruption in *ROBO1,* a gene implicated in dyslexia (Lewis et al., 2006). Shriberg (2010b) includes a summary of findings from case reports of severe speech disorders consistent with CAS in an array of genetic and complex neurodevelopmental disorders.

Statement of the Problem

A literature review indicates that despite early and compliant dietary management, more than 50% of persons with galactosemia reportedly have significant SSD consistent with CAS. However, these studies have not used well-developed or consistent criteria to diagnose CAS in GALT. Of the 13 studies reporting speech disorders in galactosemia, five used observational reports (Hughes et al., 2009; Jan & Wilson, 1973; Koch, Schmidt, Wagstaff, Ng, & Packman, 1992; Lee, 1972; Sommer et al., 1995), three used language tests (Waisbren, Norman, Schnell, & Levy, 1983; Schweitzer, Shin, Jakobs, & Brodehl, 1993; Hansen et al., 1996), two used parent questionnaires (Waggoner et al., 1990; Waggoner & Buist, 1993), two used the Apraxia Profile with a subset of participants (Robertson et al., 2000; Webb et al., 2003), and one used a checklist of speech characteristics, testing some participants in person and others by telephone (Nelson et al., 1991). Detailed study of the speech of children and adolescents with this complex neurodevelopmental disorder using well-developed contemporary methods has the potential to contribute to clinical management issues in galactosemia and to inform descriptive–explanatory accounts of the origin and nature of CAS.

In this study, we posed three questions about CAS in youth with galactosemia:

Question 1: What is the estimated prevalence of CAS in children with galactosemia and prior or persistent SSD?

Question 2: What demographic, cognitive–linguistic, or dietary management variables in persons with galactosemia are significant risk factors for CAS?

Question 3: What speech, prosody, and/or voice indices best discriminate participants with galactosemia and CAS from participants with galactosemia and other SSDs?

Method

Participants With Galactosemia

Recruitment. Potential participants with galactosemia and prior or persistent SSD were identified from responses to postal and e-mail announcements sent to patients in the University of Wisconsin—Madison Biochemical Genetics Program and to regional (Galactosemia Families of Minnesota) and national (Parents of Galactosemic Children) support groups. The announcement sought to recruit participants who met the following inclusionary/exclusionary criteria: (a) a diagnosis of classic (full expression) galactosemia; (b) prior or persistent SSD, as documented by a history of treatment for SSDs; (c) 4–17 years of age; (d) residence in the United States; (e) English as the only or first language; and (f) no history of significant hearing loss or craniofacial disorder affecting speech. Of 63 youth with galactosemia initially volunteered by their parents as potential participants, 30 were excluded for one or more of the following reasons: (a) did not have a diagnosis of the classic form of galactosemia (seven participants); (b) did not have a history of treatment for SSDs (11 participants); (c) were outside the target age range (six participants); (d) lived outside the United States (five participants); (e) first language was not English (one participant); (f) had a repaired cleft palate (one participant); (g) had moderate-to-profound

hearing loss (two participants); and (h) was unable to be scheduled due to time constraints (seven participants). The remaining 33 individuals, whose families resided in 17 different states in the midwestern, northeastern, eastern, southern, and western regions of the United States, were scheduled for assessment in their homes.

Assessment. Assessment of the 33 participants was completed over the course of two summers. During the first summer, 15 participants with galactosemia were assessed individually in a quiet room in their homes using a preliminary version of the 2010 version of the Madison Speech Assessment Protocol (MSAP) described in Shriberg, Fourakis, et al. (2010a). During the second summer, 2 years later, an additional 18 participants were tested in their homes using the current expanded version of the MSAP. All 33 participants with galactosemia were tested by the second author, an ASHA-certified speech-language pathologist with extensive experience in pediatric motor speech disorders. Parents/guardians of all participants signed an informed consent form granting permission for their child to participate in the study. Assent forms were signed by participants who were 11 years of age or older. Both forms were approved by Institutional Review Boards at the University of Wisconsin—Madison and Washington State University Spokane. The examiner spent additional time with one or both parents after administering the protocol to clarify relevant case history information.

Participants With Typical Development (TD)

Recruitment. Data from two other samples of speakers were required to address the three questions posed in this study. One need was for standardization data for all MSAP tasks from children and adolescents with typical development. Scores from participants in this reference group were used to derive age- and gender-based *z* scores for all speech, prosody, and voice measures so that between-group ES comparisons could be adjusted as needed for any age and/or gender differences in subgroup composition.

A total of 70 children in east Washington State were administered the current expanded version of the MSAP for the purposes of the present and other ongoing studies of childhood SSDs. This subset of an eventually larger database included five children of each gender within the even-numbered ages from 4 to 16 years. To be included in the database, referenced here as the TD group, parents and classroom teachers of potential participants had to have answered "no" to the following questions posed in a questionnaire: (a) "To your knowledge, has this student ever been referred for speech-language, hearing loss, or special education services?" and (b) "Do you have concerns about this student's progress in school?"As described later, all of the children in the TD group scored within the normal range on the Goldman Fristoe Test of Articulation—Second edition (GFTA–2; Goldman & Fristoe, 2000).

Assessment. The same examiner who tested the children with galactosemia (second author) administered the MSAP to each of the 70 TD reference database participants in a quiet room in his or her school. Consent and assent procedures were similar to those described previously for the participants with galactosemia.

Participants With Speech Delay (SD)

Description. The questions posed in this study also required comparison data from a group of children with speech delay of unknown origin. A data set of 25 children aged 3–6 years (Hauner, Shriberg, Kwiatkowski, & Allen, 2005) was selected for this purpose. This age range is the developmental period in which speech delay is most severely expressed. As reported in Hauner et al. (2005), conversational speech samples from these 25 children indicated significantly lower speech competence when compared to closely matched controls who had speech delay of unknown origin and who had participated in research studies over several decades. It is important to note, for their function as a comparative group for the speakers with galactosemia, that although the 25 participants in this data set had developmental psychosocial involvements, they did not have either the cognitive or motor involvements reported for children with galactosemia in the literature review.

Assessment. The 25 participants making up the SD comparison group had each been tested by a graduate student in communicative disorders in a clinical suite at the University of Wisconsin—Madison Phonology Clinic (Hauner et al., 2005). All assessments were completed several years before development of the MSAP. Therefore, the comparison data from each of these participants with severe SD were limited to perceptual and acoustic indices (to be described in a subsequent section) derived from conversational speech samples only.

The MSAP

As described previously, the same examiner assessed the participants with galactosemia and the participants with TD using the MSAP (Shriberg, Fourakis, et al., 2010a). For efficiency, the text, tabular, and graphic descriptions of the MSAP and summary findings for a perceptual and acoustic reliability estimate are included in Appendix A. The point-to-point reliability estimates were generally in the 80%–90% range, consistent with reliability estimates for perceptual and acoustic data reduction methods reported elsewhere (see Shriberg, Fourakis,

et al., 2010b). The interested reader may wish to review the protocol and methods at this point, referring to it as needed for specific information.

Competence, Precision, and Stability Analytics (CPSA)

Participant data from responses to the MSAP were organized using an analytic framework termed the *Competence, Precision, and Stability Analytics* (CPSA; Shriberg, Fourakis, et al., 2010a). Table 2 includes current CPSA entries for the three proposed subtypes of motor speech disorders in the Speech Disorders Classification System (SDCS; Shriberg, Fourakis, et al., 2010a); indices and markers for the three proposed etiologic subtypes of speech delay are in process. Technical information for the CPSA is summarized in Shriberg, Fourakis, et al. (2010a) and is presented in detail in a laboratory manual (Shriberg, Hersh, et al., 2008). The CPSA provides a theory-neutral matrix to describe, quantify, and classify SSDs and is used in the present article to address the three questions posed in the statement of purpose.

As shown in Table 2, the rows of the CPSA matrix divide MSAP findings into 10 domains subordinated under segmental and suprasegmental tiers. Segmental domains organize findings from the MSAP measures by vowels (monophthongs and diphthongs), consonants, and composite measures derived from tasks that yield indices from both vowels and consonants. The seven linguistic domains within the suprasegmental tier are subordinated within the constructs of prosody (phrasing, rate, stress) and voice (loudness, pitch, laryngeal quality, resonance), following the substantive, procedural, psychometric, and reference information in McSweeny and Shriberg (2001); Shriberg, Kwiatkowski, and Rasmussen (1990); and Shriberg, Kwiatkowski, Rasmussen, Lof, and Miller (1992).

As shown in Table 2, the columns of the CPSA matrix aggregate MSAP findings within three analytic constructs termed *competence, precision,* and *stability.* Competence indices, obtained using perceptual methods, quantify a speaker's mastery of the phonetic and phonological features of his or her ambient dialect of English. Precision indices, obtained using both perceptual and acoustic methods, quantify variance in speech, prosody, and voice production relative to speakers of the same age and gender. As described in Shriberg, Fourakis, et al. (2010a), perceptual measures of precision use diacritic symbols to capture allophonic segmental detail (e.g., a backed vowel, a spirantized stop, a partially voiced stop, a lengthened vowel, a weak stop), whereas acoustic measures provide continuous data on the precision of segmental and suprasegmental parameters (frequency, amplitude, duration, laryngeal quality, and resonance). Stability, also obtained using both perceptual and acoustic methods, quantifies consistency of speech production across multiple types, tokens, and contexts. Stability is computed by subtracting the coefficient of variation [*SD* divided by the mean] from 1.

Candidate Markers for Three Subtypes of Motor Speech Disorders

As shown in Table 2, the coded entries adjacent to each precision and stability index indicate its assignment to one of the three SDCS classifications for motor speech disorders: Motor Speech Disorder–Apraxia of Speech (MSD-AOS; equivalent to CAS), Motor Speech Disorder–Dysarthria (MSD-DYS), and Motor Speech Disorder–Not Otherwise Specified (MSD-NOS). As discussed in Shriberg, Fourakis, et al. (2010a), the addition of the third classification to the other two subtypes was deemed necessary to classify speech behaviors that are sensitive to motor speech disorder but are not specific for AOS or dysarthria. For example, imprecise speech sounds and slow rate are observed in both AOS and dysarthria. Assignments of each index to one of the three motor speech disorders in Table 2 were based on findings in both the adult AOS and CAS literatures (e.g., ASHA, 2007; Caruso & Strand, 1999; Duffy, 2005; Shriberg, Aram, & Kwiatkowski, 1997a; Shriberg & Campbell, 2003; Shriberg, Campbell, et al., 2003). Additional discussion of the rationale for marker assignment is beyond the scope of this article. As reported in Shriberg, Fourakis, et al. (2010a), 83% of the current precision and stability indices are obtained using acoustic methods. Modifications of and additions to the entries in Table 2 are expected in emerging SDCS research using the MSAP and the CPSA.

For each speech, prosody, and voice marker in Table 2, the software's task is to classify a participant as positive (affected) or negative (not affected) using a set of classification rules that includes findings from multiple CPSA indices obtained from multiple MSAP sources. A liberal statistical criterion for classifying a marker as positive was used to minimize Type II errors in which a potentially informative marker is missed due to an overly conservative statistical criterion for typically low-powered effect size (ES) estimates. Specifically, participants were classified as positive for markers in which *z* scores for the markers were lower or greater (directionality is indicated by the adjective in the marker) than 1 *SD* from the relevant reference group (TD or SD) for the question posed.

Clinical Identification of Participants With CAS

Rationale. A final methodological need was to determine the speech status of each of the participants with galactosemia relative to contemporary classification

Table 2. Competence, precision, and stability indices in the Competence, Precision, and Stability Analytics (CPSA) framework.

Ten linguistic domains	Competence	Precision		Stability	
	Title	Title	MSD	Title	MSD
		SEGMENTAL			
1. Vowels	Percentage of Non-Rhotic Vowels Correct	**Reduced Vowel Space**	NOS	**Less Stable Vowel Space**	AOS
	Percentage of Rhotic Vowels Correct	**Lengthened Vowels**	NOS	**Less Stable F1**	AOS
	Percentage of Phonemic Diphthongs Correct	**Distorted Rhotics**	NOS	**Less Stable F2**	AOS
	Percentage of Vowels Correct: CSS	**Reduced Pairwise Vowel**	NOS	**Less Stable Vowel Duration**	AOS
	Percentage of Vowels Correct: AT	**Duration Variability**		**Less Stable Rhotic Distortions: F3–F2**	AOS
	Percentage of Non-Rhotic Vowels Correct—Revised			Less Stable Vowel Errors	AOS
	Percentage of Rhotic Vowels Correct—Revised				
	Percentage of Phonemic Diphthongs Correct—Revised				
	Percentage of Vowels Correct Revised: CSS				
	Percentage of Vowels Correct Revised: AT				
	Percentage of Relative Non-Rhotic Vowel Distortions				
2. Consonants	Percentage of Consonants in Inventory	Nasal Emissions	DYS	Less Stable Consonant Errors	AOS
	Percentage of Consonants Correct: CSS	Reduced % Glides Correct	AOS	**Less Stable Sibilant Centroids**	AOS
	Percentage of Consonants Correct: AT	**Lowered Sibilant Centroids**	NOS		
	Percentage of Consonants Correct—Revised: CSS	**Lengthened Cluster Durations**	NOS		
	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 and consonants	SDCS	Increased % of Phoneme Distortions	NOS	Less Stable Whole Word Errors	AOS
	Intelligibility Index	**Syllable/Word Segregation: Increased**	NOS	Less Stable % Phonemes	AOS
	Percentage of Structurally Correct Words	**% Between/Within-Word Pauses**		Correct in Complex Words	
		SUPRASEGMENTAL			
Prosody					
4. Phrasing	Percentage Appropriate Phrasing	Increased Repetitions and Revisions	AOS	**Reduced Speech–Pause Duration Variability Ratio**	AOS
5. Rate	Percentage Appropriate Rate	**Slower Speaking Rate**	NOS	**Less Stable Speaking Rate**	AOS
		Slower Articulation Rate	NOS	**Less Stable Articulation Rate**	AOS
6. Stress	Percentage Appropriate Stress	**Reduced Lexical Stress**	NOS	**Less Stable Lexical Stress**	AOS
		Increased Lexical Stress	NOS	**Less Stable Emphatic Stress**	AOS
		Reduced Emphatic Stress	NOS	**Less Stable Sentential Stress**	AOS
		Reduced Sentential Stress	NOS		

(Continued on the following page)

Table 2 *Continued.* Competence, precision, and stability indices in the Competence, Precision, and Stability Analytics (CPSA) framework.

Ten linguistic domains	Competence	Precision		Stability	
	Title	Title	MSD	Title	MSD
Voice					
7. Loudness	Percentage Appropriate Loudness	**Reduced Vowels–Consonants Intensity Ratios**	NOS	**Less Stable Vowels–Consonants Intensity Ratios**	AOS
		Increased Vowels–Consonants Intensity Ratios	NOS		
8. Pitch	Percentage Appropriate Pitch	**Lowered Fundamental Frequency Mean**	DYS	**Less Stable Fundamental Frequency Mean**	AOS
		Raised Fundamental Frequency Mean	NOS		
		Lowered Fundamental Frequency Range	DYS		
		Increased Fundamental Frequency Range	NOS		
9. Laryngeal quality	Percentage Appropriate Laryngeal Quality	Increased Jitter	DYS	**Less Stable Jitter**	AOS
		Increased Shimmer	DYS	**Less Stable Shimmer**	AOS
		Reduced Harmonics-to-Noise Ratio	DYS	**Less Stable Harmonics-to-Noise Ratio**	AOS
		Increased % Breathy Utterances	DYS		
		Increased % Rough Utterances	DYS		
		Increased % Strained Utterances	DYS		
		Increased % Break/Shift/ Tremorous Utterances	DYS		
10. Resonance quality	Percentage Appropriate Resonance Quality	Increased % Nasal Utterances	DYS	**Less Stable: Nasal: Lowered F1: /a/**	AOS
		Nasal: Lowered F1:/a/	DYS	**Nasopharyngeal: Less Stable F2: High Vowels**	AOS
		Increased % Nasopharyngeal Utterances	NOS		
		Nasopharyngeal: Lowered F2: High Vowels	NOS		

Note. Entries in the columns indicate the interim assignment of indices to the Motor Speech Disorder (MSD) classification categories in the Speech Disorders Classification System (SDCS). Currently, there are no classification assignments for Competence indices. Bold entries indicate that candidate marker analysis was completed using acoustic data reduction methods. CPSA = Competence, Precision, and Stability Analytics; CSS = Conversational Speech Sample; AT = Articulation Test (a generic term for alternative articulation tests, including the Goldman Fristoe Test of Articulation [2nd ed.], Sounds-in-Words section); MWT = Multisyllabic Words Task; AOS = Motor Speech Disorder–Apraxia of Speech; DYS = Motor Speech Disorder–Dysarthria; NOS = Motor Speech Disorder–Not Otherwise Specified.

criteria for CAS and subtypes of dysarthria. One way to complete this task would have been to use a paneling procedure, which would yield consensus classifications from experienced judges. This approach was rejected because, as observed in Shriberg, Aram, and Kwiatkowski (1997b) and other studies using paneling methods, resulting classifications of motor speech disorder are based on heterogeneous, typically nonoperationalized diagnostic criteria. The present method was to obtain classifications from one clinician–researcher (third author) with extensive experience using a modified form of the most widely researched clinical classification system for acquired motor speech disorders, generally referenced as the *Mayo Clinic system* (Darley, Aronson, & Brown, 1975; Duffy, 2005). The modified form reflects contemporary consensus on acquired AOS and emerging consensus on CAS (e.g., Duffy, 2005; Robin et al., 2008).

Procedures. The third author used the modified version of the Mayo Clinic system adapted for pediatric motor speech disorders and the MSAP speech tasks to classify each of the 33 participants with galactosemia. Using only the information on the video (15 participants) and audio (18 participants) recordings of MSAP administrations, the third author tallied and annotated the occurrence of speech and nonspeech characteristics, including behaviors occurring during the conversational speech sample and each of the other tasks in the preliminary and expanded versions of the MSAP (see Table A1). To meet criteria for CAS, a participant had to have evidence of four of the following 10 behaviors in three or more MSAP tasks: vowel distortions, 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 diadochokinetic rates, and increased difficulty with multisyllabic words. Participants were classified as having one or more subtypes of dysarthria if they had evidence of three or more of the following nine behaviors in three or more MSAP tasks: scanning speech, equal sentential stress, sound distortions, irregular diadochokinetic rates (each of which is suggestive of ataxic dysarthria), slow rate, reduced range of motion, reduced strength of articulatory contacts, reduced respiratory support or respiratory incoordination, and strained or breathy phonatory quality. Other observations such as adventitious movement also contributed to this classification. Each of the 33 participants with galactosemia and SSD was classified as having CAS and/or dysarthria based on these contemporary clinical diagnostic criteria. Because MSD-NOS had not been developed as an SDCS classification category at the time, the third author did not have the option of using MSD-NOS for MSAP responses that were not specific for MSD-AOS or MSD-DYS or for participants whose total scores did not meet criteria for either MSD-AOS or MSD-DYS. The resulting clinical diagnostic classifications for each of the youth with galactosemia were used for each of the questions posed in this study. Findings from a reliability study of these classifications are described in Appendix A. Overall interjudge agreement for a random sample of 10 participants classified by an examiner with extensive experience in motor speech disorders was 90%.

Results

Question 1: What Is the Estimated Prevalence of CAS in Children With Galactosemia and Prior or Persistent SSD?

Prevalence of Galactosemia

Table 3 includes summary information that is organized to provide statistical analyses of prevalence data and risk factor data for participants with galactosemia (abbreviated to GALT) in the present study who did and did not meet the third author's criteria for CAS. As shown in the first column in Table 3, titled Group 1: GALT CAS, eight participants with galactosemia met the contemporary clinical diagnostic criteria for CAS described previously. One of the eight participants classified as having CAS also met the criteria described previously for dysarthria. The data from an additional participant whose speech data met only the criteria for dysarthria were removed from further analyses to restrict all analyses to questions addressing CAS. The remaining 24 participants with galactosemia were divided into two subgroups titled Group 2: GALT SD (SD = Speech Delay) and Group 3: GALT SE (SE = Speech Errors). The rationale for doing so is presented in a subsequent discussion of risk factor correlates.

Using the recruitment procedures, assessment tools, and diagnostic classification criteria described in the Method section, the prevalence of CAS in the present sample of speakers with galactosemia and prior or persistent SSD was 24% (8 of 33) or nearly one of every four participants sampled. This prevalence estimate is at the lower end of the range of CAS reported for youth and adults with galactosemia summarized in Table 1 (including the same participants in two studies assessed with different instruments), the mean of which is approximately 48%. The present prevalence estimate for CAS was expected to be higher than the percentages in Table 1 because those estimates were based on all participants with galactosemia, whereas the present study required participants with galactosemia to also have histories of a significant SSD. An estimate of the prevalence of CAS in all individuals with galactosemia who do not have other frank risk factors can be obtained by adding to the present

Table 3. Descriptive and risk factor data for 32 participants with galactosemia (one participant with ataxic dysarthria excluded) divided into three groups: Group 1: GALT CAS (n = 8), Group 2: GALT SD (n = 9), and Group 3: GALT SE (n = 15).

	Group 1: GALT CAS (n = 8)		Group 2: GALT SD (n = 9)		Group 3: GALT SE (n = 15)		Groups 1 and 2	Groups 1 and 3	Groups 2 and 3
Categorical variables	***n***		***n***		***n***		**ES**	**ES**	**ES**
Demographic									
Gender (% males)	6 (75%)		7 (77.8%)		8 (53.3%)		0.65 (–1.38, 1.50)	–0.46 (–1.72, 1.03)	–0.52 (–1.74, 0.90)
Galactosemia									
Genotype (Classic)[a]	3/3 (100%)		4/6 (66.7%)		6/13 (46.2%)		–1.23 (–2.16, 1.41)	–1.65 (–2.26, 0.96)	–0.42 (–1.80, 1.18)
Cognition									
Categorical[b] (<85)	6 (75%)		3 (33.3%)		7 (46.7%)		–0.86 (–2.18, 0.63)	–0.59 (–1.84, 0.86)	0.27 (–1.15, 1.58)
Oral facial structure (atypical)	2 (25%)		4 (44.4%)		5 (33.3%)		0.41 (–1.13, 1.84)	0.18 (–1.29, 1.46)	–0.23 (–1.59, 1.14)
Oral facial function (atypical)	8 (100%)		9 (100%)		13 (86.7%)		0.00 (–1.26, 1.31)	–0.75 (–1.38, 1.03)	–0.75 (–1.39, 0.93)
	Group 1: GALT CAS (n = 8)		**Group 2: GALT SD (n = 9)**		**Group 3: GALT SE (n = 15)**		**Groups 1 and 2**	**Groups 1 and 3**	**Groups 2 and 3**
Continuous variables	***M***	***SD***	***M***	***SD***	***M***	***SD***	**ES**	**ES**	**ES**
Demographic									
Age (months)	111.4	50.3	81.2	21.3	115.8	27.5	0.76 (–0.23, 1.75)	–0.12 (–0.97, 0.74)	**–1.31 (–2.22, –0.41)**
Mother's education (years)	14.5	1.7	14.8	1.6	16.3	2.3	–0.17 (–1.13, 0.78)	–0.82 (–1.71, 0.07)	–0.70 (–1.55, 0.15)
Father's education (years)	13.4	2.4	14.6	2.2	16.0	2.6	–0.50 (–1.46, 0.47)	**–0.99 (–1.89, –0.08)**	–0.55 (–1.39, 0.29)
Galactosemia									
Days until diagnosis	8.25	3.11	8.33	4.0	8.60	8.87	–0.02 (–0.97, 0.93)	–0.05 (–0.90, 0.81)	–0.03 (–0.86, 0.79)
Days on milk	7.13	3.64	6.89	5.42	7.87	8.83	0.05 (–0.90, 1.00)	–0.09 (–0.95, 0.76)	–0.12 (–0.95, 0.71)
Cognition									
Continuous[b]	74.8	19.4	93.3	14.4	88.3	12.8	**–1.04 (–2.05, –0.02)**	–0.85 (–1.74, 0.04)	0.36 (–0.47, 1.19)
Nonword repetition task[c]	–6.4	4.4	–2.5	1.4	–1.8	1.4	**–1.17 (–2.20, –0.14)**	**–1.59 (–2.57, –0.62)**	–0.48 (–1.32, 0.35)
Syllable repetition task[c]	–4.9	4.1	–1.9	2.2	–1.7	2.0	–0.88 (–1.88, 0.12)	**–1.07 (–1.98, –0.16)**	–0.09 (–0.92, 0.73)
Language									
Comprehension[d]	75.1	18.1	86.0	18.5	80.9	14.6	–0.56 (–1.54, 0.41)	–0.35 (–1.22, 0.51)	0.31 (–0.53, 1.14)
Language									
Expression[d]	68.8	17.5	86.2	11.8	83.6	14.2	**–1.12 (–2.14, –0.10)**	**–0.93 (–1.83, –0.03)**	0.19 (–0.64, 1.02)
Speech[e]	49.3	21.9	64.2	16.5	78.2	19.7	–0.74 (–1.72, 0.25)	**–1.36 (–2.31, –0.42)**	–0.73 (–1.58, 0.12)
Maximum phonation Time (s)	6.6	4.1	7.8	5.2	11.7	4.6	–0.24 (–1.20, 0.71)	**–1.11 (–2.02, –0.19)**	–0.78 (–1.64, 0.08)

Note. Bolded entries indicate statistically significant between-group effect sizes (ESs). See text for descriptions of each group. GALT CAS = participants with galactosemia who have childhood apraxia of speech; GALT SD = participants with galactosemia who have speech delay; GALT SE = participants with galactosemia who have speech errors.

[a]Classic Galactosemia: Q188R/Q188R. The complete genotype for participants in each of the three groups was unknown. [b]See Kaufman & Kaufman (2004). [c]z scores to adjust for age differences (see Dollaghan & Campbell, 1998; Shriberg et al., 2009). [d]See Carrow-Woolfolk, E. (1995). [e]See Goldman & Fristoe (2000).

33 participants used as the denominator in the calculation the 11 candidates with galactosemia who were excluded from participation in the present study because they did not have a history of speech disorder. The resulting percentage of 4- to 16- year-old youth with galactosemia, CAS, and none of the other risk factors used to exclude participants from the present study is 18% (8/44).

Several additional factors would support the 24% conditional prevalence percentage and the 18% unconditional prevalence percentage estimates compared to exactly twice the mean conditional estimate (48%) based on the studies in Table 1. The most likely source of difference is the more conservative contemporary clinical diagnostic criteria used to classify the eight participants as CAS in the present study, compared to the diagnostic criteria for CAS reported in studies dating back to the early 1970s. What is significant for both theory and practice is that the 18% and 24% prevalence estimates obtained in the present sample are significantly higher than estimates of the prevalence of idiopathic AOS. Compared to the population prevalence estimate of approximately 0.1% for idiopathic CAS cited previously (Shriberg & Kwiatkowski, 1994; Shriberg, Aram, & Kwiatkowski, 1997a), the present 18% unconditional estimated prevalence rate for CAS in children and adolescents with galactosemia represents an 180-fold increased risk (i.e., 18/0.1).

Question 2: What Demographic, Cognitive–Linguistic, or Dietary Management Variables in Persons With Galactosemia Are Significant Risk Factors for CAS?

Risk Factors for CAS in Youth With Galactosemia

Table 3 also includes information on demographic and risk factors associated with CAS in youth with galactosemia. Preliminary inspection of the GFTA–2 competence data indicated the need to divide the remaining 24 participants with galactosemia (i.e., those not meeting criteria for CAS) into two subgroups based on their speech status at assessment, as classified by the SDCS–Typology as updated in Shriberg, Fourakis, et al. (2010a). As shown in Table 3, the nine participants making up Group 2: GALT SD met criteria for active speech delay (children younger than 9 years of age) or persistent speech delay (individuals older than 9 years of age with residual speech sound deletions and/or substitutions [Shriberg, Fourakis, et al., 2010a]). The 15 participants in Group 3: GALT SE had a distortion-only subtype of SSD termed *Speech Errors* (SE) in the SDCS–Typology (i.e., they did not meet SDCS criteria for present or persistent speech delay). Thus, in addition to the TD database used to derive *z* scores for all perceptual and acoustic measures and the SD comparison database, two comparison groups of speakers with galactosemia (Groups 2 and 3) were included in the statistical analyses (which are described subsequently). Between-group comparisons in Table 3 included two-tailed odds ratios (based on exact .950 confidence intervals [CIs]; StatXact, Cytel Software Corporation, 2001); for the categorical variables in the first five rows, and two-tailed ESs (.950; Hedge's *g* corrected for small cell sizes) for the continuous variables (Rosenthal & Rosnow, 1991).

Demographics. The first set of risk factor questions addressed whether there were significant differences in the gender and/or mean ages of participants within the three subgroups of participants with galactosemia. Findings from these and other comparisons were also important preliminary information for subsequent analyses of dependent variables that might be sensitive to significant between-group differences in correlates of demographic composition.

As shown by the lack of bolded ESs and CIs in the rightmost three columns in Table 3, none of the three between-group comparisons for the proportion of males was statistically significant (i.e., the CIs around the mean differences include 1.00). For the age comparison in the Table 3 statistical findings for continuous variables, for which significant ESs require CIs around the mean difference that do not include zero, GALT SD participants were significantly younger than GALT SE participants (ES = –1.31). For the central upcoming comparisons between the GALT CAS and GALT SD groups, however, the mean ages of the GALT CAS participants (approximately 9 years) and the GALT SD participants (approximately 7 years) were not significantly different. Both risk-factor findings attest to the persistence of both CAS and some other type of speech disorder beyond 6 years of age in speakers with galactosemia. As indicated in Table 3, there was one significant between-group difference in the parental education levels, indicating that fathers of participants in the GALT CAS group averaged approximately 1 year less education than did the fathers of participants in the GALT SD group. Among all groups of participants with galactosemia, both parents averaged approximately 1–2 years of post–high school education.

Galactosemia. Table 3 also includes findings for three risk factors specifically associated with galactosemia. Documented genotypes were not available for all participants, limiting generalization from the nonsignificant trends in Table 3 for a higher percentage of GALT CAS participants to have the Q188R/Q188R genotype discussed previously. There were no significant between-group findings for the other two galactosemia variables (i.e., "days until diagnosis" and "days on milk"). These

findings, which indicate that GALT CAS participants were not at greater risk for CAS than participants in either of the other two speech disorder groups, are consistent with the literature consensus reviewed previously, which indicate that days on milk is not a sufficient risk factor to explain the complex neurodevelopmental challenges in persons with galactosemia, including the cognitive and CAS issues considered next.

Cognition. The continuous data findings in Table 3 comparing the cognitive status of participants in the three subgroups indicated that participants in the GALT CAS group—75% of whose composite IQs were below 85 (see Table 3)—had significantly lower composite IQs than did participants with galactosemia in the GALT SD subgroup (ES = –1.04). Findings for the two nonsense word repetition tasks (Nonword Repetition Task [NRT; Dollaghan & Campbell, 1998] and Syllable Repetition Task [SRT; Shriberg et al., 2009]) were consistent with findings for the cognitive measure (Kaufman Brief Intelligence Test, Second Edition [KBIT–2; Kaufman & Kaufman, 2004]). To adjust for the significant age difference between the GALT SD and GALT SE groups, all between-group comparisons were completed using age-adjusted *z* scores derived from the TD database. As shown in Table 3, GALT CAS participants had significantly lower average *z* scores than did the participants in the GALT SD and the GALT SE groups on the NRT (ESs = –1.17 and –1.59, respectively) and the GALT SE group on the SRT (ES = –1.07). Thus, whatever the speech processing constraint(s) underlying lowered performance on nonsense word repetition tasks (i.e., constraints in phonological encoding, memory, and/or transcoding [cf. Shriberg, 2010c; Shriberg et al., 2009]), the participants in this study had significantly lower scores than did children with typical development of similar age, with greater deficits statistically confirmed for participants with galactosemia and CAS.

Language. As shown in Table 3, there were no significant between-group differences in any of the three comparisons of scores on the Oral and Written Language Scales (OWLS; Carrow-Woolfolk, 1995) receptive language scale. On the OWLS expressive language scale, however, the scores of the GALT CAS group were significantly lower than those of both the GALT SD (ES = –1.12) and the GALT SE (ES = –0.93) subgroups.

Orofacial structure and function and phonation time. Finally, Table 3 includes findings for two variables scored categorically, orofacial structure and function, and one variable scored continuously, maximum phonation time. There were no significant between-group differences for orofacial structures and function as screened with the assessment procedure described in Appendix Table A1. Participants in the GALT CAS group, who were not significantly younger than participants in the GALT SD group, had phonation times that were significantly shorter than those of GALT SE participants (ES = –1.11).

Summary

The data in Table 3 are interpreted as supporting a prevalence rate for CAS in children and adolescents with galactosemia of 18%–24%. This finding is consistent with prior reports indicating that CAS is highly prevalent in galactosemia but at less than half the approximately 48% average rate in the prior studies shown in Table 1. This difference in obtained prevalence estimates is likely associated with many methodological differences between the present and prior studies, particularly in the more stringent diagnostic criteria for CAS used in the present study compared with those used in prior studies. The risk findings support prior reports of cognitive and expressive language challenges in participants with galactosemia, with those participants in the present study who meet the criteria for CAS being significantly more affected.

These risk factor data do not support significant differences from typical development in orofacial structure or function in any of the three groups of participants with galactosemia and SSDs, but these data did identify significantly shorter than typical phonation times in the GALT CAS participants. A forthcoming report will focus on this latter finding and on other aspects of sensorimotor speech processing in the three groups of participants with galactosemia, using data from several movement measures not included in the present article. Findings from additional examination of the present risk-factor findings are reviewed in a later summative discussion.

Question 3: What Speech, Prosody, and/or Voice Indices Best Discriminate Participants With Galactosemia and CAS From Participants With Galactosemia and Other SSDs?

Competence Indices Findings

Competence indices in the CPSA framework quantify severity of involvement. It is efficient to report detailed findings for this construct in Appendix B. Unlike findings for precision and stability, in which the statistical approach provides evidenced-based, percentage of positive marker analyses, results for competence are analyzed through use of conventional groupwise comparisons and ES statistics. Findings from these between-group analyses reported in Appendix B may be summarized as follows: (a) vowel indices: GALT CAS participants had significantly lower competence in this domain in conversational speech than did both the GALT SD participants

and the participants with SD; (b) consonant indices: GALT CAS participants scored significantly lower than did the GALT SD group on 33% of the consonant indices from continuous speech and on the GFTA–2; (c) indices that include both vowels and consonants: GALT CAS participants had significantly lower competence than did GALT SD participants on the percentage of spoken words that retain the intended number of sounds and syllables in words; and (d) prosody–voice indices: GALT CAS group participants had significantly lower scores than did the SD group on 57% of the suprasegmental measures, including indices of rate, stress, pitch, and resonance. Appendix B provides detailed tabular and text descriptions of all between-group statistical competence comparisons; these findings are integrated into the Discussion section.

Precision and Stability Indices Findings

Rationale for the percentage of positive markers metric. The dependent variables for the between-group competence analyses in Appendix B are mean scores on each of the 30 indices of speech competence. The dependent variables for the present between-group analyses of precision and stability indices are each subgroup's mean percentage of positive motor speech disorder markers (i.e., at least 1 *SD* greater in the expected direction than the average score of TD speakers matched on age and gender). Rationale for this metric is the assumption that probabilities of disorder increase in proportion to the number of candidate signs (i.e., diagnostic markers) of the disorder on which they test positive. Such additive, scalar approaches to measurement in complex disorders are used when there is no one (or more) well-validated biomarker or behavioral marker pathognomonic for the disorder and when the disorder is expressed as a syndromic-like complex of signs. As described next, whereas competence metrics in the CPSA are used to quantify severity of expression of a disorder, the percentage of positive markers metric is used to classify putative etiologic subtypes of SSD.

Statistical design. Table 4 and Figures 1 and 2 provide summaries of the analyses of candidate markers of the three SDCS motor speech disorder classifications: MSD-AOS (synonymous with CAS), MSD-DYS, and MSD-NOS. For exploratory purposes, a fourth, composite set combining markers from MSD-AOS and MSD-NOS was also derived and was termed *MSD-AOS/NOS*. The descriptive statistics in Table 4 and the graphic illustrations in Figures 1 and 2 summarize average percentages of positive markers for each participant subgroup: GALT CAS, GALT SD, GALT SE, GALT SD/SE (a composite group to be described later), and SD. Horizontal brackets between subgroups in Figures 1 and 2 indicate significant (or marginally significant) differences in the average percentage of positive markers for each comparison. As just noted, for exploratory purposes, and in consideration of power limitations, marginally significant ESs in which the lower boundary of the CI crossed zero by .003 or less are shown without the conventional asterisk indicating statistical significance at the .05 alpha level. Figures 1 and 2 differ by the sources used for data on each set of measures. The data for all groups in Figure 1 were obtained from all available MSAP sources, whereas the data for all groups in Figure 2 were obtained from only conversational speech samples (i.e., the only data available from the SD group).

Table 4. Descriptive statistics for the Percentage of Positive Markers obtained for the 57 precision and stability markers in the CPSA analytic framework.

			MSD classification							
	Source		MSD-AOS		MSD-DYS		MSD-NOS		TOTAL MSD-AOS/NOS	
Participant group	All	CS	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*
GALT CAS	X		51.5	12.6	17.4	20.0	69.4	14.4	59.4	9.9
		X	30.1	17.1	13.0	15.9	57.4	15.3	42.3	10.3
GALT SD	X		42.4	11.3	18.4	11.4	63.8	11.7	51.5	11.3
		X	27.8	10.6	17.3	10.6	48.7	14.1	36.7	10.0
GALT SE	X		41.2	16.8	19.0	11.3	60.1	10.7	49.6	16.8
		X	28.7	13.3	12.3	10.5	48.6	14.6	37.4	10.0
GALT SD/SE	X		41.7	14.7	18.8	11.1	61.5	10.9	50.3	10.3
		X	28.3	12.1	14.2	10.6	48.6	14.1	37.2	9.8
SD		X	30.7	12.2	20.8	19.7	38.8	13.2	34.0	7.2

Note. See text and relevant tables for description of participant groups, motor speech subtypes, sources, and markers.

Figure 1. Percentage of positive marker findings for participants in the three galactosemia subgroups. See text for descriptions of the motor speech markers, data sources, and rationale for combining subgroups in the four right-hand panels. MSD-AOS = Motor Speech Disorder–Apraxia of Speech; GALT CAS = participants with galactosemia who have childhood apraxia of speech; GALT SD = participants with galactosemia who have speech delay; GALT SE = participants with galactosemia who have speech errors; MSD-DYS = Motor Speech Disorder–Dysarthria; MSD-NOS = Motor Speech Disorder–Not Otherwise Specified; MSD-AOS/NOS = Motor Speech Disorder–Apraxia of Speech/Not Otherwise Specified.

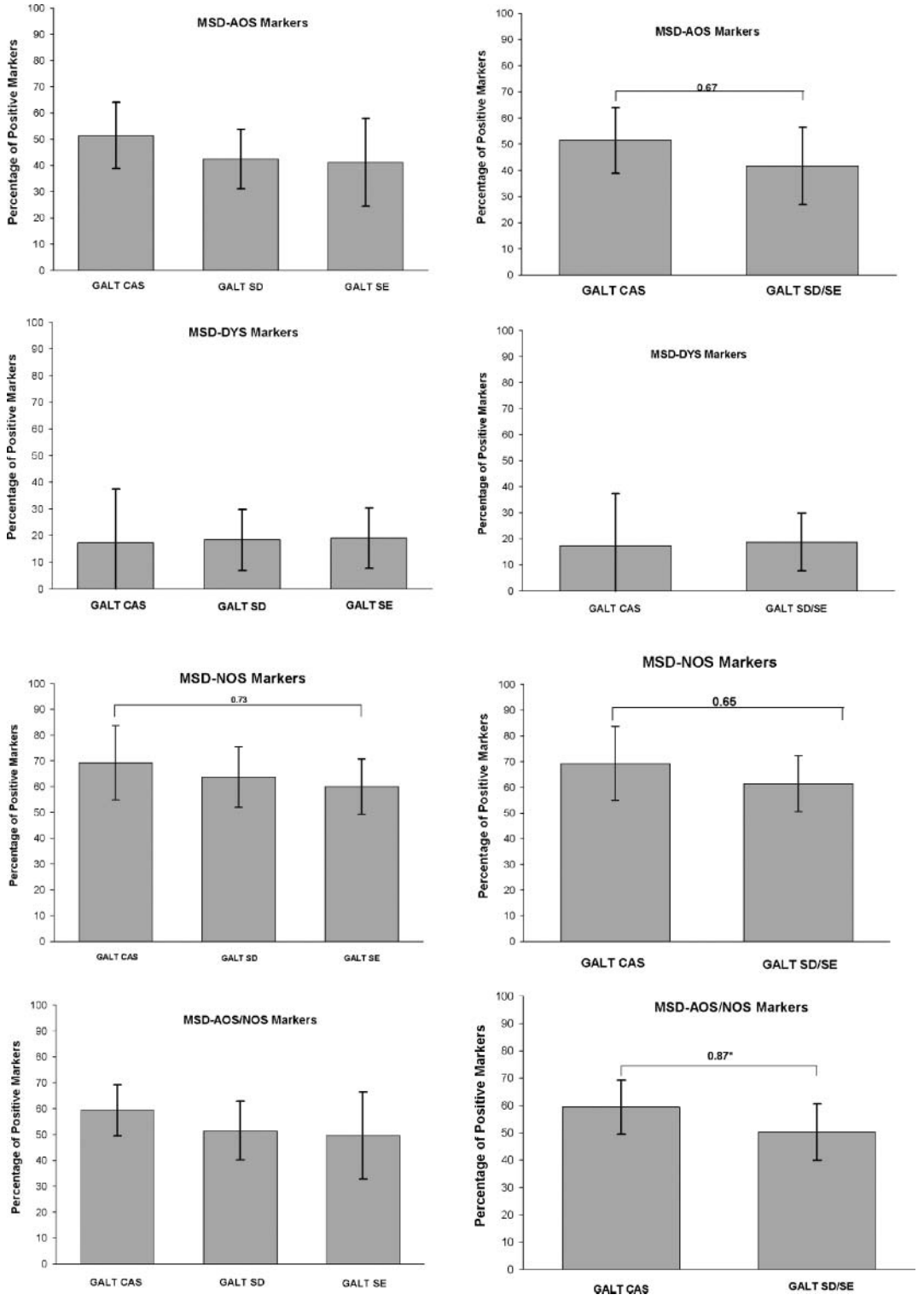
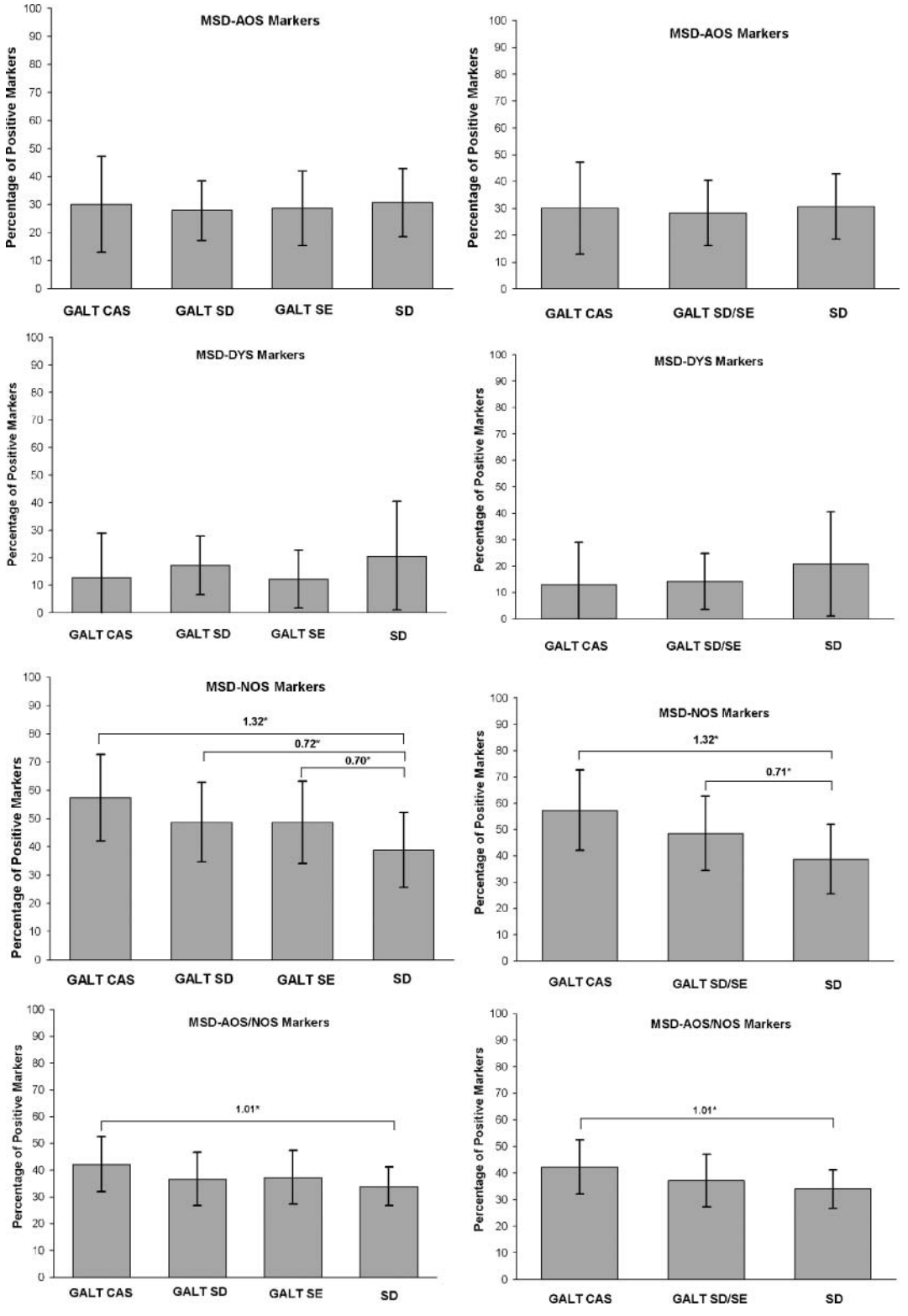


Figure 2. Percentage of positive marker findings for participants in the three galactosemia subgroups and the speech delay participants. All findings are limited to data from the conversational speech samples; see text for descriptions of the speech markers and rationale for combining subgroups in the four right-hand panels.



Marker Findings Among Galactosemia Subgroups

The percentage of positive markers comparisons shown in the four panels on the left side of Figure 1 include only one marginally significant difference. GALT CAS participants had a marginally higher percentage of positive MSD-NOS markers than did GALT SE participants (ES = 0.73; see Table 4 for all means and *SD* values). Otherwise, the lack of significant between-group differences between GALT CAS and each of the other two galactosemia subgroups was viewed as support for combining the latter two subgroups to constitute one larger comparison subgroup of all 24 participants termed *GALT SD/SE*. The assumption was that the increased statistical power created by pooling all galactosemia participants with a speech disorder other than CAS would have greater sensitivity to true differences in the average percentages of positive markers by participants with and without CAS.

As shown in the middle-right panel in Figure 1, GALT CAS participants did not differ from the GALT SD/SE group on the average percentage of the markers considered to be positive for MSD-DYS. As shown in the other three panels on the right side of Figure 1, however, comparisons of the combined GALT SD/SE group and the GALT CAS group yielded two marginally significant and one significant between-group finding. The GALT CAS participants had marginally higher percentages of positive MSD-AOS markers than did the GALT SD/SE group (ES = 0.67) and marginally higher percentages of positive MSD-NOS markers (ES = 0.65). As indicated in the lower right panel, GALT CAS participants had significantly higher percentages of the combined MSD-AOS/NOS markers than did galactosemia participants without CAS (ES = 0.87).

Marker Findings Between Galactosemia Groups and the SD Group

The eight panels in Figure 2 are similar in format to those in Figure 1. As indicated in the bottom row of Table 4, these analyses were completed using only the information on precision and stability markers available from the conversational speech samples of participants in each of the four groups. As shown in the four left-hand panels in Figure 2, there were no significant or marginal between-group ESs for the 25 MSD-AOS markers and for the 12 MSD-DYS markers obtained solely from the conversational speech samples. For the MSD-NOS markers, however, participants in all three galactosemia groups had significantly higher percentages of positive markers than did participants in the SD group. Significant ESs for the three comparisons with the SD participants, respectively, were GALT CAS: ES = 1.32, GALT SD: ES = 0.72, and GALT SE: ES = 0.70. GALT CAS participants also had a significantly higher percentage of positive markers for motor speech disorder than did participants in the SD group on the 45 combined MSD-AOS/NOS markers (ES = 1.01).

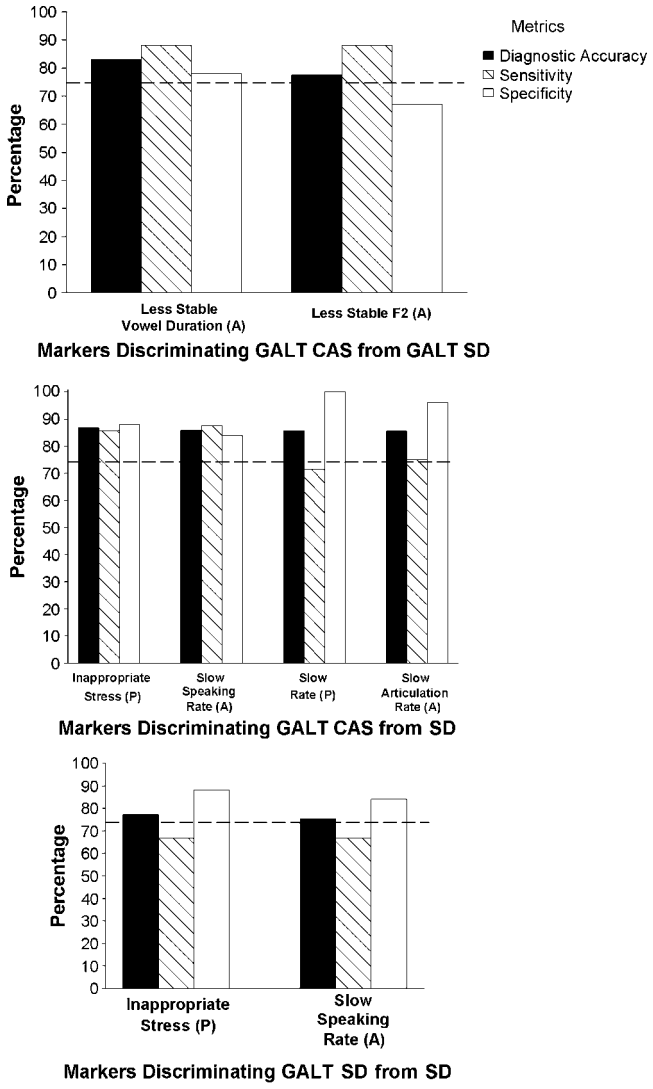
As there were no significant or marginal differences in the percentage of positive markers for motor speech disorder between the GALT SD and GALT SE groups, their marker data from conversational speech samples were combined for the analyses summarized in the four right panels in Figure 2. As shown, the larger cell size of the merged GALT SD/SE group did not increase the number of significant between-group differences when compared to the marker data obtained for the noncombined SD and SE groups.

Promising Diagnostic Markers of CAS

The final analyses series inspected the individual marker data to identify competence, precision, and stability indices with the highest potential to accurately identify CAS. Findings are shown in Figure 3. As indicated by the dashed line in each panel in Figure 3, 75% was selected as the lower limit of diagnostic accuracy, but a few markers close to this arbitrary criterion for behavioral measures were included in Figure 3. The leftmost bar indicates the obtained diagnostic accuracy of a potential marker, defined as the sum of the target group's true positive participants and the comparison group's true negative participants, divided by the sum of the true positives, true negatives, false positives, and false negatives multiplied by 100. The other two bars for each of the nine markers in Figure 3 indicate the marker's sensitivity to CAS (true positives) and its specificity relative to the comparison group (true negatives). Within each comparison panel, the markers are sequenced left to right by the magnitude of the percentage of diagnostic accuracy (solid filled bars) and include information on the method of data reduction (A = acoustic; P = perceptual). The data in the top panel were obtained using all eligible sources; comparisons with the SD group (middle and bottom panel) were obtained only from the conversational samples of each group.

Markers best differentiating GALT CAS from GALT SD. As indicated previously, the most informative control for the GALT CAS group is the GALT SD group because both groups have galactosemia, speech delay, and cognitive deficits. The top panel in Figure 3 includes two speech production indices with promising diagnostic ability to differentiate MSD-AOS from speech delay in the context of possible MSD-NOS: the CAS markers known as *less stable vowel duration* (diagnostic accuracy = 83%; sensitivity = 88%; specificity = 78%) and *less stable F2* (diagnostic accuracy = 77.5%; sensitivity = 88%; specificity = 67%). Both stability measures, each assigned to

Figure 3. Competence, Precision, and Stability indices with the highest diagnostic accuracy for MSD-AOS. See text for criteria for diagnostic accuracy for the three subgroup comparisons. P = perceptual; A = acoustic.



MSD-AOS on the basis of the precedent literatures in AOS and idiopathic CAS, were obtained using acoustic methods.

Markers best differentiating GALT CAS from SD. The middle panel in Figure 3 provides diagnostic accuracy findings for four measures that discriminated the participants with GALT CAS from those with SD. Although of paramount interest for research and clinical applications, constraints in the present comparison of CAS to SD limit generalizations. Again, differences in cognitive status are an important possible confound for at least some potential diagnostic markers, and the limitation of analyses to conversational speech data for this comparison constrains the sensitivity and, possibly, specificity of these analyses.

As shown in the middle panel in Figure 3, Inappropriate Stress, scored perceptually, was the most discriminating marker of GALT CAS participants compared to participants with galactosemia and SD (diagnostic accuracy = 86.9%; sensitivity = 85.7%; specificity = 88.0%). The second and third most discriminatory markers, quantified using acoustic and perceptual methods, respectively, were Slow Speaking Rate (i.e., includes pauses, in comparison with Slow Articulation Rate, which does not) and Slow Rate. Diagnostic accuracy for Slow Speaking Rate was 85.8% (sensitivity = 87.5%; specificity = 84%), and diagnostic accuracy for Slow Rate was 85.7% (sensitivity = 71.4%; specificity = 100%). The fourth most discriminating marker was Slow Articulation Rate, which was measured using acoustic methods (diagnostic accuracy = 85.5%; sensitivity = 75%; specificity = 96%). As described, the latter measure of articulation rate subtracts all pauses from speaking rates and, thus, is presumed to better index speech execution time.

Markers best differentiating GALT SD from SD. Findings for a third diagnostic accuracy analysis address the question posed previously of whether children with galactosemia and speech delay, but not CAS, have some type of motor speech disorder (i.e., MSD-NOS). As shown in the bottom panel of Figure 3, there were two measures in conversational speech that marginally met the 75% diagnostic accuracy criterion for this comparison: Inappropriate Stress, scored using perceptual methods (diagnostic accuracy = 77.3%; sensitivity = 66.7%; specificity = 88%), and Slow Speaking Rate, scored using acoustic methods (diagnostic accuracy = 75.3%; sensitivity = 66.7%; specificity = 84%). Notice that these findings negate the middle panel findings in Figure 3 indicating that Inappropriate Stress and Slow Speaking Rate might be used to differentiate CAS from SD because both the GALT CAS and GALT SD groups had higher percentages of speakers with Inappropriate Stress and Slow Speaking Rate compared to the percentages for participants with SD.

Discussion

Methodological Constraints

Some methodological constraints warrant comment before discussion of findings. First, the small cell sizes for the galactosemia groups clearly constrain the reliabilities of means and variance estimates for the risk factor data in Table 3 and for all descriptive statistics used in the speech competence, precision, and stability analyses. This common limitation in studies of rare disorders was addressed in the present study by combining

groups when statistically warranted (e.g., Figures 2 and 3). Although the consistency of the present findings of high prevalence of CAS and other motor speech disorders in galactosemia with findings in the precedent literature suggests that the small sample was likely representative, cross-validation studies are needed.

A second methodological constraint, noted several times, is the limitation in the sensitivity of information from the participants with SD due to the lack of complete MSAP data. Analyses of MSAP data from the present and other data sets indicate that speakers may be two to three times more likely to be positive for motor speech indices in contexts other than conversational speech. For example, vowel space is routinely smaller when assessed in conversational speech than in citation speech (examples of the latter include the CVC citation forms in Vowel Task 1 [VT1]; see Table A1), likely constraining the sensitivity of continuous speech samples to potentially significant between-group differences in vowel space. This sampling constraint was noted in Odell and Shriberg (2001), which updated findings from a prior research series in CAS (Shriberg, Aram, & Kwiatkowski, 1997a, 1997b, 1997c). Specifically, the latest article of the three noted that the 1997 study series likely underestimated the numbers of true positive participants with CAS because all speech data for those analyses were based on conversational speech samples only.

A third methodological constraint in the present study was the use of a relatively liberal classification criterion for positive markers. The present criterion of a score below 1 *SD* from the age- and gender-matched reference data may require more conservative adjustment to increase specificity among subtypes of pediatric motor speech disorders. Post hoc examination of findings suggests that for the goals of the present study and other studies using the SDCS, this criterion was more appropriate for sensitivity/specificity goals than was the use of a more stringent criterion—for example, 1.20 *SD*s or greater. Additional study is needed on the optimum cut points in the distributions of scores in target and reference data, which will require increased numbers in both sets of reference data used in the present study—MSAP data from TD speakers and from speakers with SD.

A final challenging methodological constraint is the circularity inherent in bootstrap designs such as those used in the present study. The arbitrary inclusionary and exclusionary criteria used to classify participants with CAS are as much of a design constraint in the present study as arbitrary criteria are in all other studies of CAS. Guyette and Diedrich (1981) and McNeil, Robin, and Schmidt (1997) are widely cited discussions of this circularity problem in the literatures of CAS and adult AOS, respectively. In the present study, classification of CAS by the third author was accomplished using a set of 10 putative diagnostic markers requiring an arbitrary number of positive occurrences on an arbitrary number of speech tasks. It is possible that these criteria produced some false positives for CAS, and possibly some false negatives, due to the lack of additional, diagnostically relevant information (e.g., motor speech examinations) available in the video and/or audio recordings of participants' responses to the MSAP. The premise of the present design is that the classification criteria used in the present study have sufficient validity (face, consensual, construct, concurrent) to yield study groups with an adequate number of true positives (GALT CAS) and true negatives (GALT SD, GALT SE, SD) for CAS to bootstrap to the next level of fine-grained quantitative study of promising diagnostic markers.

Prevalence of AOS in Galactosemia

For the first question posed in this report, findings indicated that CAS was highly prevalent (18%) in a sample of youth with galactosemia when adjusted for the present inclusionary criteria requiring active or prior SSD. This estimate is just over one third the approximately 48% average prevalence rate reported in the most methodologically robust studies of CAS in galactosemia (see Table 1) and is 180 times larger than the 0.1% estimated population prevalence of idiopathic CAS (Shriberg, Aram, & Kwiatkowski, 1997a). Both of the latter prevalence estimates date back to prior decades, when the use of CAS classification methods differed considerably from those used in the present study. As suggested previously, a reasonable premise is that the present lowered prevalence estimate for CAS in youth with galactosemia (approximately 1 in 5 [20%] compared with 1 in 2 [50%]) is, at least in part, due to the more stringent inclusionary criteria used in the present article to differentiate CAS from severe speech delay.

In addition to findings supporting a high prevalence of CAS in galactosemia, the present findings support a high prevalence of some other form(s) of motor speech disorder in this rare metabolic disorder. The finding that the GALT SD and GALT SE participants had significantly higher percentages of positive motor speech markers compared with participants in the SD control group (see Figure 3) is viewed as central to goals of understanding the developmental neurobiology underlying the neurocognitive and neuromotor deficits reported in youth with galactosemia despite well-managed dietary histories.

Risk Factors for and Correlates of AOS in Galactosemia

The second question addressed in this study was whether participants classified as positive for CAS (GALT

CAS) differed significantly from participants in the other two galactosemia groups (GALT SD and GALT SE) on available risk factors for or correlates of galactosemia (see Table 3). The small cell sizes, missing genotype information, and minimal clinical data for participants limited the type and power of analytic approaches to this question. Of the 14 variables for which statistical data were available (see Table 3), statistically significant ESs indicating that GALT CAS participants were younger and had fathers with approximately 1 year less education than participants in one of the other subgroups may be sampling errors and are not viewed as relevant for explanatory models of CAS. Significant ESs indicating that GALT CAS participants had lower maximum phonation times than participants in the other two galactosemia groups, however, might be an important clue to an eventual account of the pathophysiologies underlying CAS and/or dysarthria in galactosemia. As noted, a forthcoming article will address speech motor control findings for the present participants with galactosemia, including phonation time and other speech findings, within a larger set of motor movement measures not included in the present report.

The six significant findings indicating that GALT CAS participants averaged lower cognitive and expressive language scores than did participants in one or both of the other two groups are viewed as central to both explanatory models of AOS and other motor disorders in galactosemia and for the development of effective treatment options. Explanatory models are divided on whether comorbid deficits in two or more related developmental domains (e.g., speech development, language development, motor development) confer risk for one another or have common antecedents. As noted previously, cell size limitations in the present database prohibit the types of multivariate analyses that could be used to address such questions.

Statistical limitations notwithstanding, the lack of clear between-group differences among the categorical and continuous galactosemia variables summarized in Table 3 is especially notable. As discussed previously, there were too many missing data on genotypes to assess whether the homogeneous Q188R genotype was associated with higher risk for CAS. Also, there was no support for orofacial structure or function risk factors or correlates of CAS in this sample of youth with galactosemia. For the potential risk factors for CAS of "days until diagnosis" and "days on milk," however, the descriptive and inferential statistics clearly suggest no significant differences or trends. A recent study of 59 participants with *Duarte galactosemia,* which is a less severe form of galactosemia than the classic form reviewed here, also found developmental issues in a statistically significant number of participants, despite galactose restriction until 1 year (Powell et al., 2009).

Diagnostic Markers of CAS and Other Pediatric Motor Speech Disorders

The third study question addressed what many investigators have underscored as the primary need in CAS research—what speech, prosody, and/or voice features are sensitive to and specific for this subtype of motor speech disorder? The goal of identifying one or more highly sensitive and specific biomarkers for CAS is consistent with contemporary research goals in diseases and complex neurodevelopmental disorders. We have suggested that the pursuit of this goal is aided by dividing potentially pathognomonic behavioral markers for CAS into the three clinical categories for pediatric motor speech disorders used in the present study—MSD-AOS, MSD-DYS, and MSD-NOS. Given its high co-occurrence with other subtypes of motor speech disorders (Shriberg, 2010b) and high comorbidity with language impairment, it is unlikely that any one behavioral measure will be highly specific for CAS at all levels of severity and at all ages throughout the lifespan. Some final observations address the potential utility of the SDCS for research in CAS as it occurs in neurological, neurodevelopmental, and idiopathic contexts.

First, relative to the previously mentioned goal, there was no one speech, prosody, or voice marker with high diagnostic accuracy for CAS (i.e., nominally, > 90%). As shown in Figure 3, the two markers with the highest diagnostic accuracy in the present study were Less Stable Vowel Duration (diagnostic accuracy = 83.0%) and Less Stable F2 (diagnostic accuracy = 77.5%). The two markers share three characteristics: vowel targets, deficits in stability, and acoustic indices. The inclusionary criterion for the classification of CAS in the present study requiring vowel errors is an obvious constraint on these findings. However, inspection of the inclusionary data indicated that there were no participants who met the criteria for vowel errors who did not also meet the other token count/task criteria for CAS. High occurrence of vowel errors has been reported in all widely cited studies of CAS (ASHA, 2007). To our knowledge, however, the present findings provide the first quantitative support for deficits in both spatial and temporal vowel stability as promising candidates for pathognomonic speech markers of CAS in 4- to 16-year-old youth.

Second, this article reports the first use of the MSD-NOS classification category introduced in Shriberg, Fourakis, et al. (2010a). Findings support its productivity as a placeholder for both potential diagnostic markers of CAS and for participants who do not meet specificity criteria for the other two MSD classifications but have speech characteristics and other risk factors not observed in participants with any form of SD of currently unknown origin. One possible clinical dividend from this working term is its potential to reduce the widely reported

overdiagnosis of CAS (ASHA, 2007). Although features such as slow rate and reduced vowel space may be sensitive to motor speech disorder, they should not be included on "checklists" of speech behaviors that purport to be specific for CAS. Rather, children with only such characteristics may have some type of motor immaturity, with implications for intervention and prediction of normalization that differ from those in AOS and for the several subtypes of dysarthria. As reviewed in Shriberg, Fourakis, et al. (2010a), there is a significant need for systematic studies of pediatric motor speech disorders leading to a well-validated nosology.

Last, the methodological constraints reviewed previously and the limitation of the application of the present findings to those in only one complex neurodevelopmental disorder preclude generalizations about CAS as a possible idiopathic disorder. However, there is one puzzling finding in the present data that might be interpreted as countersupport for the perspective of a core set of CAS markers across neurologic, neurodevelopmental, and idiopathic contexts. In prior studies of children with idiopathic CAS, we have reported two acoustic indices with high diagnostic accuracy for CAS: inappropriate lexical stress (Shriberg, Aram, & Kwiatkowski, 1997b, 1997c; Shriberg, Campbell, et al., 2003) and reduced variability in speech time relative to pause time durations (Shriberg, Green, Campbell, McSweeny, & Scheer, 2003). In the present study of youth with galactosemia and CAS, neither index had high diagnostic accuracy. Although there are some measurement differences that may be relevant, a more likely source of the failure to replicate prior findings would seem to be associated with participant characteristics in the prior studies of participants with idiopathic CAS compared to those in the present study of participants with a metabolic disorder. Research in progress is using SDCS methods described in Shriberg, Fourakis, et al. (2010a) and in the present article to profile CAS in diverse neurological, neurodevelopmental, and idiopathic contexts. Again, we defer research and clinical generalizations from the present findings to research and clinical issues in these other contexts for CAS until empirical findings are available and cross-validated.

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Appendix A (p. 1 of 6). Assessment methods and reliability estimates.

Some of the information in this appendix was reported in Shriberg, Fourakis, et al. (2010a). These authors report three extensions to the SDCS: (a) an extended nosology for MSD; (b) the MSAP; and (c) the CPSA. Detailed information on these and other elements of the SDCS are provided in an unpublished document known as the *Phonology Project Laboratory Manual* (Shriberg, Hersh, et al., 2008). Basic information on the software environment for all SDCS data reduction and statistical analyses is provided in Shriberg, Allen, McSweeny, and Wilson (2001). The following sections provide information on assessment and data reduction methods used in the present study, a summary of an estimate of the reliability of the methods, and findings from an estimate of the reliability of motor speech classification assignments completed by the third author.

Data Collection and Reduction Methods

Structure and Content

Table A1 and Figure A1 provide information on the structure and content of the MSAP. Table A1 includes brief descriptions of the goals of all MSAP measures and the number and types of constituent stimuli in the 15 MSAP tasks that assess a speaker's speech, prosody, and voice. The tests and tasks in Table A1 were selected from relevant literatures or were developed over several decades in a research program in pediatric SSDs at the University of Wisconsin—Madison. The fixed sequence of task administration was determined to optimize examiner efficiency and examinee compliance, particularly with young children or speakers who are difficult to assess. As shown in Table A1, four variants of the MSAP protocol are used to accommodate differences in speakers' ages, following methods developed by Lewis and colleagues (e.g., Stein et al., 2006).

Figure A1 illustrates the diversity of sampling contexts for the 15 MSAP speech tasks. Responses are obtained using both imitative and spontaneous evocation modes, in linguistic units that include sounds, syllables, words, and utterances, and in simple and complex phonetic and phonological contexts. The structure and content of speech data obtained with the MSAP were designed to provide information on the competence, precision, and stability of participants' speech production. As indicated previously, additional information on the MSAP is available in Shriberg, Fourakis, et al. (2010a) and is documented in an unpublished research manual, the *Phonology Project Laboratory Manual*. The laboratory manual includes extensive information and instructions on data collection, perceptual and acoustic data reduction, and data analyses using a series of software tools.

Administration

The auditory stimuli for most of the imitative speech tasks described in Table A1 were presented by computer with some of the stimuli accompanied by colorful illustrations. Gamelike activities and cumulative incentives were used to obtain and sustain attention and motivation to complete the protocol in one or two assessment sessions, individualized to the attention span and interests of each participant.

Instrumentation and Data Reduction

Recording instrumentation. Recordings for the three data sets described in the text were made in quiet environments in participants' homes, educational facilities, and clinical research facilities. Speech samples for the first series of participants with galactosemia were recorded on a Sony DCR-DVD301 digital video recorder using a Shure WH30TOG cardiod microphone. Samples for the second galactosemia series and the TD reference database were recorded on a Marantz CDR 420 digital audio recorder and a Shure MX412D/C microphone. Speech samples for the participants with SD were originally recorded using a Sony 5000 audiocassette recorder and a Teac ME-50 microphone. They were subsequently digitized using a Tascam 112MK II tape deck connected to Computer Speech Lab 4300B (CSL4300B) hardware. The signal was sampled at 20 kHz with 16 bits of quantization using the CSL 4300B record facility.

Playback instrumentation. All audio playback, transcription, and prosody-voice coding procedures for the participants with speech delay are described in Hauner et al. (2005). Data reduction procedures for all other groups were accomplished using laptop computers configured with custom audio players in the Programs to Examine Phonetic and Phonological Evaluation Records (PEPPER; Shriberg et al., 2001) environment (described later in this appendix). The custom player provided waveform displays of both the audio stimuli and participant responses. Playback for acoustic analyses was also accomplished within PEPPER using a software suite developed from an Active X version of TF32 (Milenkovic, 2000).

Perceptual methods. Two perceptual methods were used to reduce speech data from the participants with galactosemia and from the comparison participants with TD and with SD. For the segmental information from the current participants with galactosemia and with TD, one of two experienced research specialists transcribed all participants' responses to each of the MSAP speech tasks using the narrow phonetic transcription symbols and conventions described in Shriberg and Kent (2003). The transcribers followed extended guidelines in the laboratory manual for research transcription in the PEPPER environment (Shriberg et al., 2001). The manual includes procedural information on glossing, formatting, and transcribing each of the 15 MSAP speech tasks. Transcription of participant responses were checked for clerical errors and keyboarded for computer analyses by a research assistant following procedures described in the manual.

The same two research specialists who transcribed the galactosemia and TD datasets used a prosody-voice screening procedure (Shriberg et al., 1990) and extended guidelines in the laboratory manual to code speakers' prosody-voice characteristics in conversational speech. These data also were checked for clerical errors and were entered into PEPPER by the research assistant. Similar procedures were used by other transcribers to transcribe and prosody-voice code the 25 children with SD (Hauner et al., 2005).

Acoustic methods. Acoustic analyses of the data from each of the three participant groups were completed by one of three analysts using instructions for segmentation, formant analyses, and spectral analyses described briefly in Shriberg, Fourakis, et al. (2010a) and in detail in the laboratory manual. Shriberg, Fourakis, et al. includes examples of the screen displays that enable high-throughput acoustic analyses. Efficiencies are gained by subroutines that automate entering and storage of acoustic values and use the stored data for the acoustic indices to be described. Unlike transcription and prosody-voice coding, for which one transcriber completed all tasks for a participant, acoustic analysts worked on a per-task basis in which each analyst was responsible for a subset of the MSAP task analyses completed on all participants.

Reliability Estimate: Data Reduction

Extensive estimates of intrajudge and interjudge agreement for transcription, prosody-voice coding, and acoustic analyses of the galactosemia and TD datasets were obtained to assess the reliability of methods used in the SDCS (Shriberg, Fourakis, et al., 2010b). Detailed methods and agreement data available in the Shriberg, Fourakis, et al. report are summarized here.

Method

Speech samples from five of the 32 (16%) participants with galactosemia were randomly selected for agreement analyses, with the requirement that three of the five participants be classified as CAS by the third author. Speech samples from five children in the TD standardization database were also randomly selected from among those participants with the greatest number of responses to MSAP tasks and the largest number of errors (younger participants). The two original transcribers each retranscribed the 10 participants' responses to five of the 15 (33%) MSAP speech tasks selected to sample the range of complexity of speech tasks in the protocol (see Table A1). As described in Shriberg, Fourakis, et al. (2010b), the five tasks, in order of mean percentage of agreement complexity (i.e., not articulatory complexity), were Vowel Task 1 (Shriberg, Fourakis, et al., 2010a), the Goldman Fristoe Test of Articulation—Second Edition (Goldman & Fristoe, 2000), the Lexical Stress Task (Shriberg, Fourakis, et al., 2010a), the Conversational Speech Sample (Shriberg, Fourakis, et al., 2010a), and the Challenging Words Task (Shriberg, Fourakis, et al., 2010a). Thus, the same randomly selected participant responses to items in each of the five MSAP tasks were used for estimates of the reliability of phonetic transcription, prosody-voice coding (based only on the conversational speech task), and acoustic analyses methods. Intrajudge and interjudge agreement estimates were completed by repeated data reduction several months to over a year following the original data reduction. Interjudge transcription included a second transcriber/prosody-voice coder and one to three acoustic analysts. Point-to-point percentages of agreement at several levels of detail were computed for transcription and prosody-voice coding by a software utility (PEPAGREE; Shriberg & Olson, 1988); acoustic analyses agreement estimates were completed manually using the procedures described in Shriberg, Fourakis, et al. (2010b).

Results

Reliability estimates were as high or higher than reliability findings reported in prior reviews of the literature and reliability estimates using perceptual methods developed in our laboratory (Shriberg & Kent, 2003; Shriberg et al., 1992; Shriberg & Lof, 1991; McSweeny & Shriberg, 1995, 2001). Averaged across speaker groups, intrajudge phonetic transcription agreement across the five MSAP tasks (including phonemes transcribed as omissions) averaged 91.5 and 96.5 for broad transcription of vowels and consonants, respectively, and 85.9 and 91.8 for narrow transcription of vowels and consonants. Interjudge transcription agreement across the five MSAP tasks (including items transcribed as omissions) averaged 85.0 and 93.2 for broad transcription of vowels and consonants, respectively, and 77.6 and 86.7 for narrow transcription of vowels and consonants. Intrajudge transcription agreement for the percentage of Prosody-Voice Screening Profile (PVSP)–coded utterances (Shriberg et al., 1992) with appropriate phrasing, stress, rate, loudness, pitch, laryngeal quality, and resonance ranged from 82.2 to 100 ($M = 93.9$). Interjudge agreement at the screening level of "appropriate" or "inappropriate" for these seven prosody and voice domains ranged from 83.1 to 99.2 ($M = 93.2$). In general, transcription agreement was as much as 10% higher for speakers in the TD group than for participants with galactosemia; however, as indicated in Shriberg, Fourakis, et al. (2010b), reliability estimates for the acoustic analyses were similar for the TD and galactosemia samples.

As indicated previously, detailed descriptions of the methods and variables used to estimate interjudge and intrajudge acoustic analyst agreement from the present datasets are provided in Shriberg, Fourakis, et al. (2010b). Essentially, intrajudge and interjudge analyst agreement estimates were obtained for segmenting phonemes (in ms), editing fundamental frequency tracking (in Hz), and formant measurement (in Hz) using linear predictive coding and visual information on screen displays. Reliability for these tasks ranged from a few mid-70% values to 100%, with most estimates in the mid-80% to mid-90% range.

Reliability Estimate: Classification of CAS

Method

Ten participants (30%) with galactosemia were randomly selected from the original 33 participants to estimate the interjudge reliability of the criteria used to classify participants as having CAS and/or dysarthria. A second random sample with replacement was completed to ensure that all classification categories assigned by the third author were represented in the reliability estimate. A clinical investigator with extensive experience in motor speech disorders was familiarized with the speech, prosody, and voice criteria used to classify participants with galactosemia as having one or both types of motor speech disorder. Using the classification criteria and all recorded responses to the MSAP tasks completed by the 10 randomly selected participants with galactosemia, the comparison judge classified the speech status of each of participant.

Results

Overall interjudge classification agreement was 90%. The comparison judge agreed with the original judge on seven of the eight participants classified as having speech disorder but not motor speech disorder. The comparison judge classified the remaining participant (who was originally classified as having speech disorder but not motor speech disorder) as having "mild CAS/artic." The comparison judge's classifications of the remaining two participants with motor speech disorder were identical to those completed by the third author. One participant was classified as having CAS by both judges, and the other was classified as having both CAS and dysarthria by both judges. These findings were interpreted as providing reliability support for the classification system for motor speech disorder used in the text.

Appendix A (p. 3 of 6). Assessment methods and reliability estimates.

Table A1. The 25 tests and tasks in the Madison Speech Assessment Protocol (MSAP).

Measure	Speech task	Acronym	Age group[a]				Description and goal	Stimuli
			1	2	3	4		
Goldman Fristoe Test of Articulation—Second Edition[b]	X	GFTA–2	X	X	X		The Sounds-in-Words section of the GFTA–2 provides supplementary production phonology information at the single-word level.	34 picture plates (53 target words).
Audiological and (optionally) Acoustic Immittance Screening Task[c]		None	X				Audiologic and acoustic immittance screening data provide status on hearing and middle ear functioning at the time of assessment and supplement case history information.	Pulsed pure tones presented at 500, 1000, 2000, and 4000 Hz at 20 dB for the audiologic screening.
Conversational Speech Sample	X	CSS	X	X	X	X	The CSS is the primary data source for production phonology, including segmental and suprasegmental (PVSP) data. It can also be used to obtain language production data.	If needed, pictures or books are used to evoke spontaneous conversational speech.
Lexical Stress Task	X	LST	X	X	X	X	The LST provides perceptual and acoustic information on a participant's ability to realize lexical stress in two-syllable words produced in imitation in a carrier phrase.	24 pictured two-syllable words (e.g., *chicken*), including 8 trochees, 8 iambs, and 8 spondees; recorded stimulus for each word in the carrier phrase "Say ____."
Challenging Words Task	X	CWT	X	X	X	X	The CWT provides information on a participant's ability to correctly sequence and produce sounds in 12 challenging words containing a variety of consonants (mostly Early- and Middle-8 sounds) and vowels in imitation. Multiple repetitions provide information on the stability of productions.	12 pictured words (e.g., *helicopter*), each presented 3 times; recorded stimulus for each token.
Vowel Task 1	X	VT1	X	X	X	X	VT1 provides information on the four corner vowels /i,æ,u,ɑ/ in single words produced in imitation. Multiple repetitions provide information on the stability of productions.	4 pictured CVC words (e.g., *bat*), each presented 4 times; recorded stimulus for each token.
Vowel Task 2	X	VT2	X	X	X	X	VT2 provides information on the 11 noncorner vowels and diphthongs in single words produced in imitation. Multiple repetitions provide information on the stability of productions.	11 pictured CVC words (e.g., *bite*), each presented 4 times; recorded stimulus for each token.
Vowel Task 3	X	VT3		X	X	X	VT3 provides information on vowels in five sentences produced in imitation. Multiple repetitions provide information on the stability of productions.	5 pictured sentences (e.g., *"He has a blue pen"*), each presented 4 times; recorded stimulus for each token.

(Continued on the following page)

Table A1 *Continued.* The 25 tests and tasks in the Madison Speech Assessment Protocol (MSAP).

Measure	Speech task	Acronym	Age group[a]				Description and goal	Stimuli
			1	2	3	4		
Syllable Repetition Task		SRT	X	X	X	X	The SRT provides information on speech processing in two- (CVCV), three- (CVCVCV), and four-syllable (CVCVCVCV) nonsense words using four Early-8 consonants /b,d,m,n/ and a single low back vowel /a/ to minimize articulatory challenges.	Recorded stimulus for each of the 18 nonsense words (e.g., /*bamana*/).
Nonword Repetition Task[d]		NRT	X	X	X	X	The NRT provides information on speech processing using nonsense words.	Recorded stimulus for each of 16 nonsense words—four each of 1-syllable, 2-syllable, 3-syllable, and 4-syllable words (e.g., /tēīvakl/)
Emphatic Stress Task	X	EST	X	X	X	X	The EST provides information on a participant's ability to realize emphatic stress within short sentences. In each of the four trials for each of two sentences, a different word is stressed.	Recorded stimuli for two 4-word sentences (e.g., *"May I see PETE"*), repeated 4 times each.
Rhotics and Sibilants Task	X	RST		X	X	X	The RST provides information for /r/ and /s/ productions obtained in imitated single words embedded in the carrier phrase "Say ____ again."	Recorded stimuli for 10 words (e.g., *soon, bird*), each repeated four times.
Multisyllabic Words Task 1	X	MWT1	X	X			MWT1 provides information on single words selected to represent difficult articulatory sequences. It assists in evaluating phonological planning, sound sequencing, and transitions from one sound to another. The MWT1 includes 25 single words for children age 3;0 to 11;11 (years;months).	Recorded stimulus for each of 25 words (e.g., *animal*).
Multisyllabic Words Task 2	X	MWT2			X	X	See description for MWT1. MWT2 includes 20 single words for participants age 12;0 and older.	Recorded stimulus for each of 20 words (e.g., *emphasis*).
Speech Phrases Task[e]	X	SPT	X	X	X	X	The SPT provides information on 25 two- and three-word phrases selected to represent difficult articulatory sequences. It assists in evaluating phonological planning, sound sequencing, and transitions from one sound to another.	Recorded stimulus for each of 25 phrases (e.g., *big farm house*).

(Continued on the following page)

Table A1 *Continued.* The 25 tests and tasks in the Madison Speech Assessment Protocol (MSAP).

Measure	Speech task	Acronym	Age group[a]				Description and goal	Stimuli
			1	2	3	4		
Diadochokinesis Task	X	DDK	X	X	X	X	The DDK task provides information on a participant's ability to coordinate rapid, accurate, and rhythmic alternating movements of the lips and tongue within a single place of articulation and across two and three places of articulation (bilabial, alveolar, and velar).	Two 1-consonant syllable strings (e.g., *papapa*), three alternating 2-consonant syllable strings, one alternating 3-consonant syllable string, and the word *pattycake*.
Sustained Vowel Task	X	SVT	X	X	X	X	The SVT provides information on a participant's respiratory–laryngeal capacity and laryngeal quality.	The vowel /a/.
Sustained Consonant Task	X	SCT	X	X	X	X	The SCT provides information on a participant's respiratory–laryngeal capacity.	The consonant /f/.
Orofacial Examination Task[f]		OET	X	X			The OET provides information on the structure and function of the speech mechanism.	None.
Oral and Written Language Scales[g]		OWLS	X	X	X	X	The OWLS provides information on language comprehension and production.	Two books of picture plates, one each for the comprehension and production subtests.
Woodcock–Johnson III Tests of Achievement[h]		WJ–III				X	The WJ–III provides information on language skills in adults in the areas of Letter–Word Identification (Test 1) and Word Attack (Test 13). (Optional tests include Test 7 [Spelling], Test 9 [Passage Comprehension], and Test 11 [Writing Samples]).	Test 1: Single letters and increasingly difficult words (e.g., *provincial*) are displayed for participants to pronounce. Test 13: Single letters and increasingly difficult nonwords (e.g., *fronkett*) are displayed for participants to pronounce.
Kaufman Brief Intelligence Test—Second Edition[i]		KBIT–2	X	X	X	X	The KBIT–2 provides information on cognitive functioning using scores from the test's three verbal and nonverbal subtests.	Two books of picture plates are used for all of the nonverbal and some of the verbal test items.
Case History Form		CHF	X	X	X	X	The CHF provides risk factor information on a participant's medical, social, academic, hearing, family aggregation, and speech-language history.	None.

(Continued on the following page)

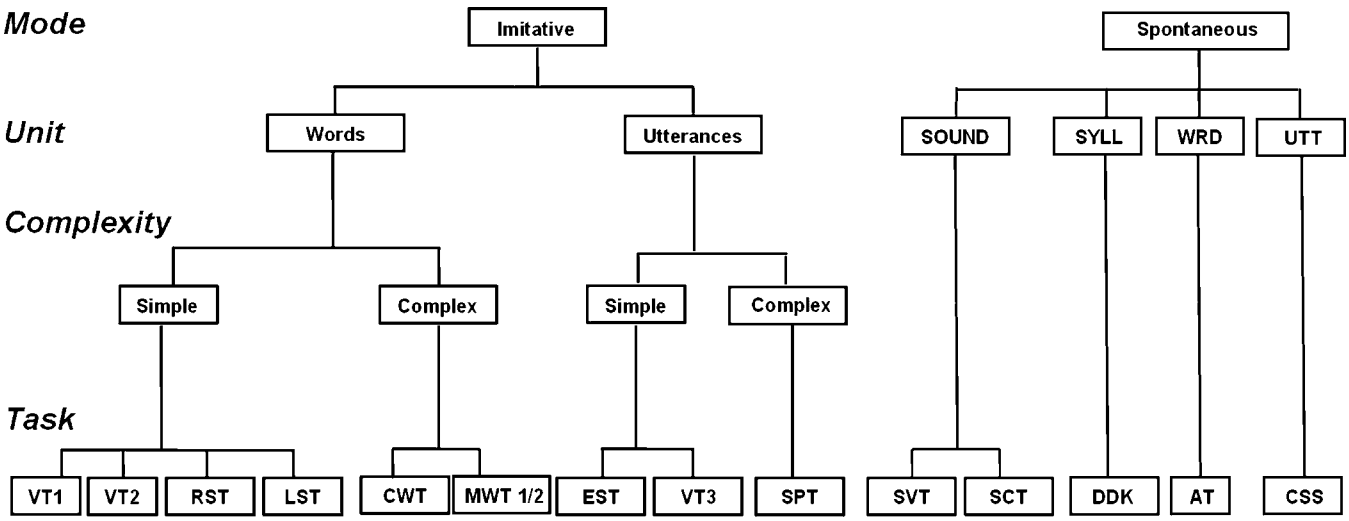
Table A1 *Continued.* The 25 tests and tasks in the Madison Speech Assessment Protocol (MSAP).

Measure	Speech task	Acronym	Age group[a] 1	2	3	4	Description and goal	Stimuli
Case History Interview		CHI	X	X	X	X	The CHI supplements and clarifies the information collected on the participant's CHF.	None.
Examiner Checklist		EC	X	X	X	X	The EC provides information on the examiner's impressions of selected aspects of the participant's behavior and psychosocial development/ affect.	None.

Note. PVSP = Prosody-Voice Screening Profile.

[a]Age group1: Preschool = 3;0–5;11; Age group 2: School-age = 6;0–11;11; Age group 3: Adolescent = 12;0–17;11; Age group 4: Adult = 18;0+. [b]See Goldman & Fristoe (2000). [c]See American National Standards Institute (1989). [d]See Dollaghan & Campbell (1998). [e]See Catts (1986). [f]For the present study, all 33 participants were administered a modified version of the OET. [g]See Carrow-Woolfolk (1995). [h]See Woodcock, McGrew, & Mather (2001). [i]See Kaufman & Kaufman (2004).

Figure A1. The Madison Speech Assessment Protocol (MSAP) speech sampling context hierarchy. SYLL = syllables; WRD = words; UTT = utterances; VT1 = Vowel Task 1; VT2 = Vowel Task 2; RST = Rhotics and Sibilants Task; LST = Lexical Stress Task; CWT = Challenging Words Task; MWT 1/2 = Multisyllabic Words Task 1/2; EST = Emphatic Stress Task; VT3 = Vowel Task 3; SPT = Speech Phrases Task; SVT = Sustained Vowel Task; SCT = Sustained Consonant Task; DDK = Diadochokinesis Task; AT = Articulation Test; CSS = Conversational Speech Sample.



Appendix B (p.1 of 5). Competence indices findings.

As indicated in the text, Competence indices in the CPSA framework are reduced using perceptual methods (phonetic transcription, prosody-voice coding). Competence indices are used to quantify and describe differences in speakers' severity of involvement, a process that is essentially independent of typologic or etiologic type of involvement. Thus, competence indices (e.g., Percentage of Consonants Correct) generally do not have the required sensitivity and specificity to be markers of SSD subtypes. However, they do provide information that is useful for descriptive–explanatory accounts of disorder subtypes and for clinical decision making.

This appendix includes descriptive statistics (*M*s, *SD*s) and inferential statistics (ESs, CIs) for between-group comparisons among the three subgroups of youth with galactosemia and the 25 participants in Group 4: Speech Delay. Between-group comparisons of Group 3: GALT SE with the other two groups were not completed for the segmental indices because the inclusionary criterion for Group 3 was speech errors (i.e., not speech delay). However, comparisons were completed for the seven prosody-voice competence indices because prosody-voice status has been shown to be independent of speech status (Shriberg et al., 1992). ES comparisons for GALT CAS and GALT SD used the raw scores for all measures because the prior analyses indicated no difference in the gender and age distributions of participants in the two groups. Raw scores were also used for the comparisons of GALT CAS with participants in the SD group (Group 4) to provide a robust test of the speech competence of GALT CAS participants. Recall that compared with the participants in the three galactosemia subgroups, the 25 participants with SD were considerably younger but had typical cognitive and motor speech development.

All between-group comparisons to be reported tested the directional hypothesis that participants in the GALT CAS group have lower speech, prosody, and/or voice competence compared with participants in the other three groups and that the GALT SD group has lower scores than participants in the GALT SE and SD groups. To address the problem of potential Type II errors due to the small cell sizes in this study, each between-group comparison was treated as a familywise effect without correction for multiple tests. The statistical significance of obtained ESs was assessed using directional, one-tailed .90 alpha levels (Rosenthal & Rosnow, 1991). Significant findings (i.e., confidence intervals not crossing zero and in the predicted direction) in Table B1 appear in boldface.

Segmental Competence Findings

Vowels

Results for the 11 monophthong and diphthong vowel measures in Table B1 (measures 1–11) indicated that the GALT CAS participants had significantly lower competence in this domain in conversational speech than both the GALT SD participants and participants with SD. Of the 20 between-group vowel indices comparisons (GFTA–2 [Articulation Test] data were not available for the SD group), significant ESs in the expected direction were obtained for eight of the 11 (73%) GALT CAS and GALT SD comparisons and for four of the nine (44%) GALT CAS and SD comparisons. Significant ESs, indicating that GALT CAS participants had lower competence on vowel measures compared with participants in both of the speech delay groups, ranged from –0.88 to –1.94.

Consonants

GALT CAS participants scored significantly lower than the GALT SD group on three of the nine (33%) measures of consonant production in conversational speech and on the GFTA–2 (see Table B-1, measures 12–20). Significant ESs for these comparisons on Percentage of Consonants Correct, Percentage of Consonants Correct—Revised, and Percentage of Consonant Correct in Complex Words ranged from –0.89 to –0.90. There were no significant between-group differences in the consonant competence of GALT CAS and SD participants. Thus, as shown by the *M*s and *SD*s for all measures in Table B1, consonant mastery of the GALT CAS group, whose average age was 9 years, was lower than or not significantly different from that of the SD participants, who were half their age (*M* = 4.5 years).

Vowels and Consonants

The three indices in Table B1 derived from both vowels and consonants (measures 21–23) provide additional information on speech mastery. Of the six between-group comparisons, the only significant ES obtained indicated that the GALT CAS participants had significantly lowered competence compared with GALT SD participants on the Percentage of Structurally Correct Words (ES = –1.02), which indexes the percentage of spoken words that retain the intended number of sounds and syllables. Importantly, GALT CAS participants were not classified as having more severe subtypes of speech delay on the SDCS–Typology subscale (Shriberg, Fourakis, et al., 2010a) than participants in the other two groups with speech delay, nor were they less intelligible in conversational speech quantified by the Intelligibility Index (Shriberg, 1993). This indicates that their consonant productions were not less competent at the phonemic and allophonic level using the perceptual methods described in the text.

Suprasegmental Competence Findings

The descriptive and inferential statistical findings in Table B1 for the seven prosody-voice domains include comparisons of the GALT CAS group to participants of the same approximate age in the GALT SE group. Suprasegmental development as coded using the PVSP has been shown to be significantly associated with motor speech disorder (McSweeny & Shriberg, 2001). For each of the seven of 21 (33%) significant between-group comparisons, with ESs ranging from –0.79 to –1.52, PVSP subcodes were inspected to determine the predominant type of inappropriate prosody or inappropriate voice (e.g., whether inappropriate rate was too slow or too fast). It is important to underscore that many of the perceptually based PVSP subcodes do not meet customary point-to-point intrajudge and interjudge agreement levels, requiring supportive findings from acoustic measures of the same domain.

GALT CAS participants were not significantly lower than GALT SD participants on any of the seven between-group comparisons of prosody and voice domains in Table B1. It is interesting to note that GALT SD participants had notably poorer laryngeal quality than GALT CAS participants, but the one-tailed directional tests summarized in Table B1 do not permit examination of this finding. GALT CAS participants had significantly lower scores than the GALT SE group on three of the seven (43%) suprasegmental measures: Percentage of Utterances With Appropriate Stress (ES = –0.82; predominantly excessive/equal misplaced stress); Percentage of Utterances With Appropriate Loudness (ES = –1.12; no predominant direction between too soft or too loud); and Percentage of Utterances With Appropriate Resonance (ES = –0.90; predominantly nasopharyngeal resonance). The GALT CAS group also had significantly lower scores than the SD group on four of the seven (57%) suprasegmental measures: Percentage of Utterances With Appropriate Rate (ES = –1.52; predominantly too slow); Percentage of Utterances With Appropriate Stress (ES = –1.03; predominantly excessive/equal misplaced stress); Percentage of Utterances With Appropriate Pitch (ES = –0.79; no predominant direction); and Percentage of Utterances With Appropriate Resonance (ES = –1.21; predominantly nasopharyngeal resonance).

These suprasegmental data support prior literature findings in CAS indicating that deficits in rate, stress, and resonance quality (differences in loudness and pitch were small in absolute magnitude) are frequent and persistent. The finding that such behaviors were also characteristic of participants in the GALT SD subgroup (i.e., scores for this subgroup were relatively low [see Table B1] and not significantly different from scores for the GALT CAS participants) supports the presence of some type of persistent suprasegmental deficit in the participants with galactosemia who had speech disorder but who did not meet criteria for CAS.

Appendix B (p. 2 of 5). Competence indices findings.

Table B1. Descriptive and inferential statistical findings for the 30 competence indices obtained from the three subgroups of participants with galactosemia (Groups 1, 2 and 3) and the comparison group of participants with Speech Delay (Group 4).

Tier	Domain	No.	Speech, Prosody, and Voice Competence Indices Title	Group 1: GALT CAS (*n* = 8)		Group 2: GALT SD (*n* = 9)		Group 3: GALT SE (*n* = 15)		Group 4: Speech Delay (*n* = 25)		1–2	1–3	1–4
				M	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	ES	ES	ES
Segmental	Vowels	1	Percentage of Non-Rhotic Vowels/ Diphthongs Correct	85.0	9.4	96.4	2.7	98.3	1.6	94.7	3.3	**–1.70 (–2.62, –0.73)**		**–1.82 (–2.58, –1.04)**
		2	Percentage of Rhotic Vowels/Diphthongs Correct	25.6	38.6	38.2	35.4	60.6	45.8	6.5	21.0	–0.34 (–1.14, 0.47)		**0.73 (0.04, 1.41)**
		3	Percentage of Phonemic Diphthongs Correct	78.0	22.8	93.5	11.1	98.9	2.2	89.0	15.4	**–0.88 (–1.71, –0.02)**		–0.63 (–1.31, 0.05)
		4	Percentage of Vowels/ Diphthongs Correct	83.1	9.6	94.3	2.3	96.1	3.8	91.6	3.2	**–1.66 (–2.57, –0.69)**		**–1.59 (–2.32, –0.83)**
		5	Percentage of Vowels/ Diphthongs Correct: AT	67.8	18.6	87.5	4.2	93.1	6.0	—	—	**–1.51 (–2.40, –0.57)**		—
		6	Percentage of Non-Rhotic Vowels/ Diphthongs Correct Revised	85.8	9.4	96.7	2.7	98.5	1.6	95.8	2.9	**–1.62 (–2.53, –0.67)**		**–1.94 (–2.71, –1.15)**
		7	Percentage of Rhotic Vowels/Diphthongs Correct Revised	73.1	21.1	68.8	22.5	91.2	14.8	40.4	36.5	0.20 (–0.61, 0.10)		**0.97 (0.27, 1.66)**
		8	Percentage of Phonemic Diphthongs Correct Revised	78.4	22.8	94.3	10.0	98.9	2.2	9.03	14.6	**–0.92 (–1.76, –0.07)**		**4.13 (3.02, 5.20)**
		9	Percentage of Vowels/ Diphthongs Correct Revised	85.3	9.5	95.7	2.5	98.0	2.0	94.0	3.4	**–1.54 (–2.44, –0.60)**		**–1.61 (–2.34, –0.85)**
		10	Percentage of Vowels/ Diphthongs Correct Revised: AT	72.7	16.9	90.6	5.1	96.6	3.3	—	—	**–1.48 (–2.37, –0.54)**		—

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Table B1 *Continued.* Descriptive and inferential statistical findings for the 30 competence indices obtained from the three subgroups of participants with galactosemia (Groups 1, 2 and 3) and the comparison group of participants with Speech Delay (Group 4).

Tier	Domain	No.	Speech, Prosody, and Voice Competence Indices Title	Group 1: GALT CAS (*n* = 8)		Group 2: GALT SD (*n* = 9)		Group 3: GALT SE (*n* = 15)		Group 4: Speech Delay (*n* = 25)		1–2	1–3	1–4
				M	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	ES	ES	ES
		11	Percentage of Relative Non-Rhotic Vowel/ Diphthong Distortions	13.0	22.4	12.7	15.1	15.0	21.2	19.5	22.0	0.02 (–0.78, 0.82)		–0.29 (–0.96, 0.38)
	Consonants	12	Percentage of Consonants in Inventory	87.2	14.7	92.9	7.8	98.9	2.7	80.6	15.4	–0.49 (–1.30, 0.33)		0.43 (–0.25, 1.10)
		13	Percentage of Consonants Correct	68.2	19.4	81.3	8.5	91.9	6.7	61.4	11.3	**–0.90 (–1.72, –0.04)**		0.50 (–0.18, 1.17)
		14	Percent of Consonants Correct: AT	55.1	30.1	74.9	16.5	91.1	8.2	—	—	–0.83 (–1.66, 0.02)		—
		15	Percentage of Consonants Correct—Revised	73.8	17.5	85.8	8.3	96.2	3.1	68.1	12.1	**–0.90 (–1.72, –0.04)**		0.42 (–0.26, 1.09)
		16	Percentage of Consonants Correct—Revised: AT	61.1	30.5	81.6	16.7	96.4	5.1	—	—	–0.85 (–1.67, 0.00)		—
		17	Percentage of Consonants Correct in Complex Words: MWT	38.1	25.6	58.3	19.7	80.4	10.7	—	—	**–0.89 (–1.72, –0.04)**		—
		18	Relative Omission Index	37.5	17.2	25.2	11.8	25.8	21.7	33.4	14.2	0.84 (–0.01, 1.67)		0.28 (–0.40, 0.94)
		19	Relative Substitution Index	41.3	11.9	49.6	16.9	29.0	15.5	47.2	13.1	–0.56 (–1.37, 0.26)		–0.46 (–1.13, 0.22)

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Appendix B (p. 4 of 5). Competence indices findings.

Table B1 *Continued.* Descriptive and inferential statistical findings for the 30 competence indices obtained from the three subgroups of participants with galactosemia (Groups 1, 2 and 3) and the comparison group of participants with Speech Delay (Group 4).

Tier	Domain	No.	Speech, Prosody, and Voice Competence Indices Title	Group 1: GALT CAS (*n* = 8)		Group 2: GALT SD (*n* = 9)		Group 3: GALT SE (*n* = 15)		Group 4: Speech Delay (*n* = 25)		1–2	1–3	1–4
				M	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	ES	ES	ES
		20	Relative Distortion Index	21.2	13.7	25.1	12.4	45.2	26.6	19.4	11.7	–0.30 (–1.10, 0.51)		0.15 (–0.52, 0.82)
	Vowels and Consonants	21	SDCS[a]	1.75	0.71	1.44	0.53	0.33	0.49	1.68	0.47	0.47 (–0.49, 1.44)		0.13 (–0.67, 0.92)
		22	Intelligibility Index (II)	82.6	16.6	90.5	13.7	98.3	1.8	90.1	8.8	–0.52 (–1.33, 0.30)		–0.68 (–1.36, 0.10)
		23	Percentage of Structurally Correct Words	84.1	10.3	91.8	3.8	97.0	1.8	79.6	7.4	**–1.02 (–1.86, –0.15)**		0.55 (–0.13, 1.23)
Suprasegmental														
Prosody	Phrasing	24	Percentage of Appropriate Phrasing	89.2	11.4	80.3	14.9	83.9	9.8	91.3	9.1	0.67 (–0.17, 1.48)	0.51 (–0.23, 1.24)	–0.22 (–0.89, 0.45)
	Rate	25	Percentage of Appropriate Rate	81.0	23.8	85.6	23.3	92.2	9.2	98.6	2.9	–0.20 (–0.99, 0.61)	–0.72 (–1.45, 0.04)	**–1.52 (–2.25, –0.77)**
	Stress	26	Percentage of Appropriate Stress	79.8	13.0	76.5	12.9	87.5	6.9	91.2	10.5	0.26 (–0.55, 1.05)	**–0.82 (–1.56, –0.06)**	**–1.03 (–1.72, –0.32)**
Voice	Loudness	27	Percentage of Appropriate Loudness	96.3	3.8	93.1	11.2	99.2	1.7	83.5	29.5	0.37 (–0.44, 1.17)	**–1.12 (–1.88, –0.33)**	0.49 (–0.19, 1.16)
	Pitch	28	Percentage of Appropriate Pitch	99.4	1.6	98.6	2.1	99.4	1.5	100.0	0.0	0.43 (–0.39, 1.23)	0 (–0.72, 0.72)	**–0.79 (–1.47, –0.10)**

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Appendix B (p. 5 of 5). Competence indices findings.

Table B1 *Continued.* Descriptive and inferential statistical findings for the 30 competence indices obtained from the three subgroups of participants with galactosemia (Groups 1, 2 and 3) and the comparison group of participants with Speech Delay (Group 4).

Tier	Domain	No.	Speech, Prosody, and Voice Competence Indices Title	Group 1: GALT CAS (*n* = 8)		Group 2: GALT SD (*n* = 9)		Group 3: GALT SE (*n* = 15)		Group 4: Speech Delay (*n* = 25)		1–2	1–3	1–4
				M	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	ES	ES	ES
	Laryngeal Quality	29	Percentage of Appropriate Laryngeal Quality	84.4	11.9	59.7	32.5	66.7	36.5	70.6	35.7	0.98 (0.12, 1.82)	0.58 (–0.16, 1.31)	0.43 (–0.25, 1.10)
	Resonance	30	Percentage of Appropriate Resonance Quality	74.6	33.6	86.4	10.6	94.4	12.5	96.4	9.6	–0.49 (–1.29, 0.33)	**–0.90 (–1.65, –0.14)**	**–1.21 (–1.91, –0.48)**

Note. AT = Articulation Test; MWT = Multisyllabic Words Task.

[a]The SDCS (Shriberg, Austin, Lewis, McSweeny, & Wilson, 1997) is a typological system for speech sound disorders. For the present purposes, participants with one of seven subtypes of SSD were grouped into three classification subtypes coded using the following ordinal system: 0 = *Normal or Normalized Speech Acquisition;* 1 = *Normal Speech Acquisition/Speech Delay, Residual Errors 1 (Distortions Only) or Questionable Residual Errors (for Participants Younger Than 9 Years);* 2 = *Speech Delay, Residual Errors 2, or Residual Errors 3 (Includes Residual Substitutions and/or Deletions).*

Prevalence and Phenotype of Childhood Apraxia of Speech in Youth With Galactosemia

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