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# Toward Diagnostic and Phenotype Markers for Genetically Transmitted Speech Delay

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Converging evidence supports the hypothesis that the most common subtype of childhood speech sound disorder (SSD) of currently unknown origin is genetically transmitted. We report the first findings toward a set of diagnostic markers to differentiate this proposed etiological subtype (provisionally termed *speech delay-genetic*) from other proposed subtypes of SSD of unknown origin. Conversational speech samples from 72 preschool children with speech delay of unknown origin from 3 research centers were selected from an audio archive. Participants differed on the number of biological, nuclear family members (0 or 2+) classified as positive for current and/or prior speech-language disorder. Although participants in the 2 groups were found to have similar speech competence, as indexed by their Percentage of Consonants Correct scores, their speech error patterns differed significantly in 3 ways. Compared with children who may have reduced genetic load for speech delay (no affected nuclear family members), children with possibly higher genetic load (2+ affected members) had (a) a significantly higher proportion of relative omission errors on the Late-8 consonants; (b) a significantly lower proportion of relative distortion errors on these consonants, particularly on the sibilant fricatives /s/, /z/, and /ʃ/; and (c) a significantly lower proportion of backed /s/ distortions, as assessed by both perceptual and acoustic methods. Machine learning routines identified a 3-part classification rule that included differential weightings of these variables. The classification rule had diagnostic accuracy value of 0.83 (95% confidence limits = 0.74–0.92), with positive and negative likelihood ratios of 9.6 (95% confidence limits = 3.1–29.9) and 0.40 (95% confidence limits = 0.24–0.68), respectively. The diagnostic accuracy findings are viewed as promising. The error pattern for this proposed subtype of SSD is viewed as consistent with the cognitive-linguistic processing deficits that have been reported for genetically transmitted verbal disorders.

**KEY WORDS:** articulation, assessment, genetics, phenotype, phonology

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**T**his report addresses the hypothesis that the most common subtype of childhood speech sound disorder (SSD) of currently unknown origin is genetically transmitted. The primary goal of the study is to determine whether there are one or more speech features that differentiate such children from those whose speech delay may result from other possible etiologies. If one or more such features (i.e., diagnostic markers) are identified, a secondary goal is to speculate on the implications of findings for an eventual explanatory account of this proposed subtype of SSD. The next section reviews some working terms that will be used in a discussion of research needs and findings in speech genetics. We later present a framework that unifies the several levels of observation addressed in this report.

## Classification Terms

Table 1 is a list of working terms for seven putative subtypes of SSD introduced in previous reports (e.g., Shriberg, 1982, 1993, 1994; Shriberg, Austin, Lewis, McSweeney, & Wilson, 1997b), as well as two new terms. As shown in the first two columns, the stem *speech delay* is used without other affixes when no claim is made about the etiological origin of one of five proposed subtypes of speech delay (or, as indicated at the bottom of Table 1, with the prefix *undifferentiated*; i.e., *undifferentiated speech delay* [USD]). The inclusionary and exclusionary criteria for speech delay used in software (Shriberg, Allen, McSweeney, & Wilson, 2001) to categorize children's speech status are described in Shriberg (1993) and Shriberg et al. (1997b). Essentially, the inclusionary criterion for speech delay is that the conversational speech of a speaker includes age-inappropriate speech sound omission errors and/or substitution errors, although children meeting this criterion also routinely have clinical and nonclinical speech sound distortion errors (Shriberg, 1993, Appendix). In contrast, children meeting inclusionary criteria for the remaining two subtypes of speech errors do not meet inclusionary criteria for speech delay. Rather, their prior and/or current speech errors in conversation consist solely of age-inappropriate speech sound distortions limited to specific sounds or feature classes. The most prevalent such distortions in American English dialects are dentalized sibilants (/s/, /z/, and /ʃ/) and derhotacized rhotics (/r/, /ɜ:/, and /ɝ/).

When a claim is made about the etiology of speech delay, one of five etiological suffixes (preceded by a dash) is appended. As shown in Table 1, the *primary* causal origin of the first type of speech delay is posited to be genetic transmission (*speech delay-genetic* [SD-GEN]); the second subtype is proposed to be causally associated with early recurrent otitis media with effusion (*speech*

*delay-otitis media with effusion* [SD-OME]); the third is presumed to be consistent with apraxia of speech (*speech delay-apraxia of speech* [SD-AOS]); the fourth is proposed to be consistent with dysarthria (*speech delay-dysarthria* [SD-DYS]); and the fifth subtype of speech delay is hypothesized to be causally associated with developmental psychosocial involvement (*speech delay-developmental psychosocial involvement* [SD-DPI]). As above, the sixth and seventh subtypes of childhood SSDs, subsumed under the term *speech errors*, provide classification categories for speakers whose history is limited to speech sound distortions. These distortion errors occur on a restricted set of consonants and semi-vowels that are phonetically and/or phonologically challenging. Finally, whereas *USD* refers to any of the five proposed subtypes of speech delay, the term *undifferentiated speech sound disorders* is used when no distinction is made between speech delay and speech errors (see Table 1). We will return to the list of classification terms and remaining two columns in Table 1 after considering some recent issues and findings in speech genetics and related research.

## Epidemiological Issues and Findings in SSD

Accurate information on the prevalence of a disorder is needed for many contemporary methods in genetics research. There have been several large- and small-scale prevalence studies of childhood SSDs of unknown origin (see reviews in Law, Boyle, Harris, Harkness, & Nye, 2000; Shriberg & Austin, 1998), but they have used classification systems that have not made the etiological and typological distinctions between speech delay and speech errors proposed in Table 1. A recent epidemiological study that used inclusionary criteria to differentiate speech delay from speech errors estimated the point prevalence of USD

**Table 1.** Working terms for seven putative subtypes of speech sound disorder (SSD).

Subtype	Working term	Working term abbreviation	Posited primary source	Processes affected
1	Speech delay-genetic	SD-GEN	Polygenic/environmental	Cognitive-linguistic
2	Speech delay-otitis media with effusion	SD-OME	Polygenic/environmental	Auditory-perceptual
3	Speech delay-apraxia of speech	SD-AOS	Monogenic? Oligogenic?	Speech-motor control
4	Speech delay-dysarthria	SD-DYS	Monogenic? Oligogenic?	Speech-motor control
5	Speech delay-developmental psychosocial involvement	SD-DPI	Polygenic/environmental	Affective-temperamental
6	Speech errors-sibilants	SE-/s/	Environmental	Phonological attunement
7	Speech errors-rhotics	SE-/r/	Environmental	Phonological attunement
	Undifferentiated speech delay	USD	Any of 1-5	Any of 1-5
	Undifferentiated SSD	USSD	Any of 1-7	Any of 1-7

in 6-year-old U.S. children at 3.8% (Shriberg, Tomblin, & McSweeney, 1999). Because preliminary longitudinal studies cited in this report indicate that approximately 75% of preschool children with USD normalize their delay by 6 years of age, the point prevalence of USD at 3 years of age is estimated to be approximately 15%–16% (i.e.,  $3.8 \times 4 = 15.2$ ). Interpreted as the possible “incidence” of USD, this relatively high estimate has implications for models of genetic transmission (valid incidence estimates require information on individuals before the onset of disease, a requirement that is not appropriate for speech delay or other developmental disorders). An incidence rate as high as 15%–16% is exactly the proportion of children that would be expected to fall below 1 *SD* (i.e., below the 16th percentile) if the production of articulate speech is treated as a normally distributed trait (cf. Leonard, 1998). Accordingly, rather than being viewed as a speech *disorder* (with its own variance comprising a smaller distribution of speech competence scores within a larger bimodal distribution of population scores), the proposed classification term, *speech delay*, would seem most consistent with these emerging epidemiological findings. That is, speech delay is viewed as the most theoretically coherent term, with the cover term *childhood* (or *pediatric*) *SSD* meeting disciplinary requirements for research and applied needs.

There are currently no prevalence data using appropriate epidemiological methods on the proposed subtype of *SSD* that we posit is primarily due to genetic inheritance (i.e., *SD-GEN*). An estimate of the clinical prevalence of *SD-GEN* from a clinical referral sample (i.e., a convenience sample not randomly ascertained or demographically stratified) indicated that 56% of 84 children referred for intelligibility problems of unknown origin had at least one nuclear family member with a similar history (Shriberg & Kwiatkowski, 1994). If cross-validated using conventional epidemiological methods, this estimate would indicate that approximately 8.5% of preschool children (i.e.,  $0.56 \times 15.2\% = 8.5\%$ ) may have a higher genetic load consistent with a genetically transmitted form of speech delay. Even this lowered prevalence rate (i.e., compared with 15%–16% for USD), which is equivalent to approximately 1.4 *SDs* below the mean, is consistent with a view of speech acquisition as a normally distributed trait with speech delay making up the lower tail of the distribution. Disorders with such relatively high prevalence rates are consistent with models in which a small (*oligogenic*) or larger (*polygenic*) number of genetic loci (rather than a single genetic locus, i.e., *monogenic*) contribute to a quantitative trait, with perhaps one gene having a major influence.

## Methodological Issues in Speech Genetics Studies

*Phenotyping.* The major assessment need in all genetic-epidemiological studies is to classify the status and severity of involvement of the proband (the index case for a target disorder) and the proband’s biological siblings, parents, and extended family (grandparents, uncles and aunts, and cousins) relative to the target disease or disorder. In the present context, the inability to directly sample the speech of all nuclear or extended family members due to a variety of logistic and genetic confidentiality concerns has been one of the two major methodological constraints on valid diagnostic classification and phenotype description. The other problem is that even for family members who are available for testing and agree to provide both speech and blood or tissue samples, the time frame for expression of manifest speech delay limits the available information. The diagnosis of speech delay is generally not appropriate until a child is approximately 3 years of age, and as indicated above, 75% of children normalize speech delay by 6 years of age, with most of the remaining children treated for speech delay normalizing by 9 years of age (Shriberg, Gruber, & Kwiatkowski, 1994; Shriberg, Kwiatkowski, & Gruber, 1994). Thus, for most speakers with a history of speech delay, there is only a 3- to 6-year active period for its manifest expression. Due to these accessibility and/or normalization constraints on direct speech measurement of family members, investigators have relied heavily on lifetime prevalence information, as generally provided by one of the caregivers. Such case history data are typically reported at relatively broad levels of domain specificity and have been demonstrated to both overestimate and underestimate involvements in each branch of the family (Plante, Shankman, & Clark, 1996; Spitz, Tallal, Flax, & Benasich, 1997; Tomblin, Freese, & Records, 1992).

For younger and older family members who are available for direct testing, speech assessment is constrained by linguistic, psychometric, and efficiency considerations. Investigators must select, from the large number of speech production tasks and measures, assessment instruments that provide sufficiently coherent data to classify and quantify whether a person had ever been affected. Previous reports have discussed the array of conceptual and psychometric issues associated with protocol development for speech genetics research (cf. Shriberg, 1993, 2003). A major goal is to select measures that are closest to the presumed pathophysiology of a genetically transmitted subtype rather than assessment tools such as citation-form articulation tests that were developed to meet sociolinguistic definitions of handicap or disability. A review of issues and

findings led to the proposal that percentage scores reflecting the precision of speech sounds in conversation have the most biobehavioral validity for speech genetics research (Shriberg, 1993).

## Findings in Speech Genetics Studies

*Behavioral studies.* To date, the primary sources supporting a genetically transmitted subtype of speech delay are the numerous reports indicating that speech-language delay aggregates in families (see Stromswold, 1998, for a review; also Campbell et al., 2003; Choudhury & Benasich, 2003; Tallal et al., 2001). Findings indicate that from 20% to 60% of probands' family members have histories of speech-language involvement, compared with fewer than 10% in family members of control children without speech-language problems. Findings from twin studies (see Stromswold, 2001, for a review; also Viding et al., 2003; Whiteside & Rixon, 2001) and an adoption study (Felsenfeld & Plomin, 1998) also provide considerable support for the heritability of speech-language disorders. A consistent finding in this literature is that individuals with language and reading disorders have difficulties repeating nonsense words (cf. Bishop, Adams, & Norbury, 2004; SLI Consortium, 2002). Because this finding is so robust in genetic studies of verbal trait disorders, many investigators have proposed that this cognitive-linguistic processing deficit (i.e., a deficit in working phonological memory) may be the commonly inherited deficit in genetically transmitted disorders of speech, language, reading, spelling, and learning.

*Molecular genetic studies.* Six studies to date have reported molecular genetic findings, three for the subtype in Table 1 termed *SD-AOS* and three for that termed *SD-GEN*. The widely published studies of a four-generation London family have led to the identification of a susceptibility gene on Chromosome 7 (*FOXP2*) that cosegregates with an orofacial apraxia and apraxia of speech. A review of the extensive findings from this programmatic research is beyond the scope of the present report (see Fisher, 2005; Fisher, Lai, & Monaco, 2003; Marcus & Fisher, 2003; Newbury & Monaco, 2002). Two recent studies support these findings (MacDermot et al., 2004; Zeesman et al., 2004).

Three other molecular genetic findings in speech genetics have used inclusionary and exclusionary diagnostic markers as well as an array of speech phenotypes and verbal trait *endophenotypes* (variables presumably closer to the gene products than the manifest phenotype, e.g., phonological working memory as assessed by nonword repetition tasks). Articles by Lewis and colleagues report susceptibility regions on the pericentromeric region of Chromosome 3 (Stein et al., 2004) and on 7q31 (Schick et al., 2002), and Pennington and co-

investigators report risk loci on Chromosomes 6 and 15 linking SSD to dyslexia (Smith et al., 2003; Smith, Pennington, Boada, & Shriberg, 2005). Based on the strength of these findings, the Online Mendelian Inheritance in Man database has recently designated SSD as the classification entry for emerging genetic findings for this developmental disorder (Johns Hopkins University, 2000).

## A Complex Disorder Framework for SSD

Figure 1 is a graphic illustration of a research framework that ties the classificatory terms introduced in Table 1 to possible causes for each proposed subtype. Complex disorder frameworks of this type have been developed for many neurodevelopmental disorders; for a lucid discussion of conceptual and methodological issues, see Pennington (2003). The framework is used to motivate two questions posed in the current study.

*Etiological processes.* At Level I of the framework depicted in Figure 1, an SSD of currently unknown origin is proposed to reflect the interaction of risk and protective factors within and among genetic and environmental domains throughout the period of speech development. Contemporary discussions of the origins and natural history of disease and disorders, as well as discussions of priorities in genomic research and public health concerns, emphasize the interactive contributions of genetic and environmental sources to neurobiological development and health throughout the life span (e.g., Eaves & Silberg, 2003; Merikangas & Risch, 2003). Although the present focus is on *SD-GEN*, which we suspect is the most prevalent subtype of SSD, there clearly are genetic contributions to each subtype of speech delay, as speculated for the five proposed subtypes of speech delay in Table 1. Based on emerging findings in speech genetics research reviewed in detail elsewhere (Shriberg, 2004), we suspect that *SD-GEN* is transmitted as a polygenetic trait and is significantly moderated by environmental risk factors. An eventual account of these *distal* origins of atypical speech acquisition will require information at the level of neural substrates (see Figure 1) reflecting processing within many neurodevelopmental and biobehavioral domains (cf. Campbell et al., 2003).

*Explanatory processes.* At Level II (explanatory processes), the products of the interactions within and among genetic and environmental domains on neurodevelopmental substrates are posited to yield *proximal* deficits in one or more of five processing domains: *cognitive-linguistic*, *auditory-perceptual*, *speech motor control*, *psychosocial*, and *phonological attunement*. It is important to underscore that the assignment of deficits in these processes to each of the proposed subtypes of SSD shown in Table 1 and

**Figure 1.** A complex disorder framework for child speech sound disorders of unknown origin.

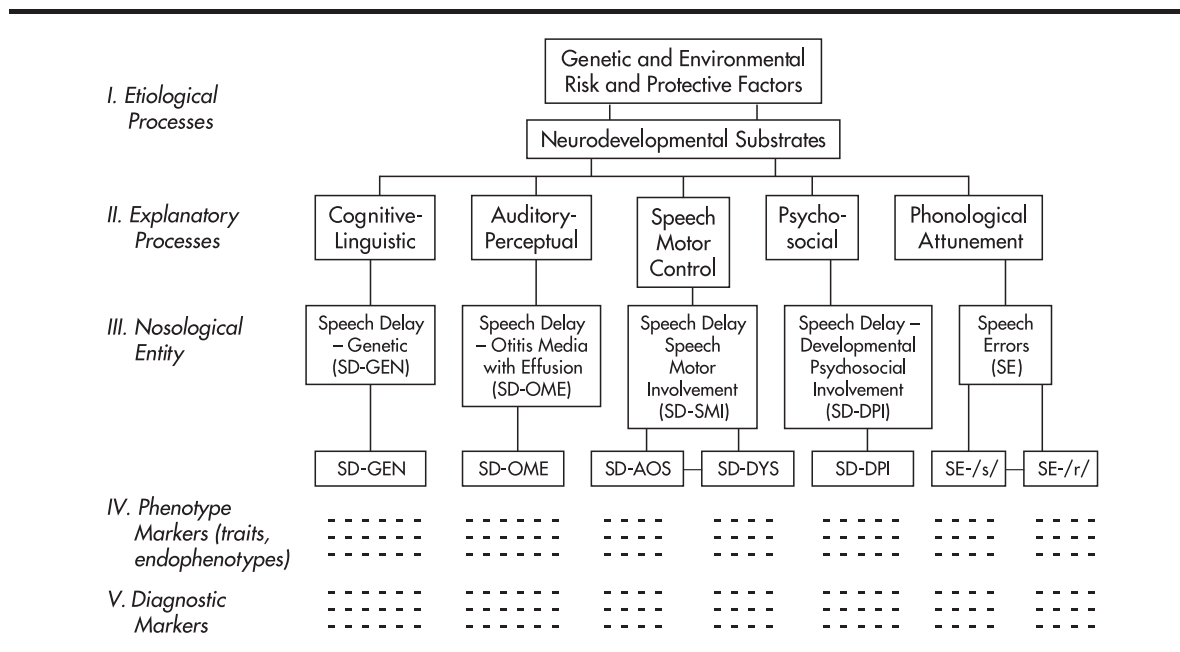


Figure 1 are speculations based on research findings (see citations below). The first four terms denote the conventional constructs associated with these domains and do not require further introductory comment. The fifth proposed explanatory construct, termed *phonological attunement*, refers to a child's disposition to respond to the environmental press for mastery of the speech sounds of the ambient language. As proposed elsewhere, the claim is that individual differences in children's attunement to the task of speech acquisition—their disposition to “tune in and tune up” (Shriberg, 1975, 1994)—underlie the acquisition of clinical and nonclinical speech sound distortions. These distortions, which are limited to certain sounds or feature classes, may possibly persist over a lifetime.

*Phenotype and diagnostic markers.* To date, phenotype (Level IV) and/or diagnostic (Level V) markers have been proposed for each of the other six etiological subtypes of SSD in this schema. The dashes in Figure 1 are placeholders both for the markers described elsewhere and for markers to be obtained. For diagnostic purposes, markers are needed that are sensitive and specific for each of the seven proposed subtypes of childhood SSDs, including SD-GEN. Recently, diagnostic markers have been proposed to discriminate among children with SD-OME (Shriberg, Flipsen, Kwiatkowski, & McSweeney, 2003; Shriberg, Kent, et al., 2003), SD-AOS (Shriberg, Campbell, et al., 2003; Shriberg, Green, Campbell, McSweeney, & Scheer, 2003), SD-DPI (Hauner, Shriberg, Kwiatkowski, & Allen, 2005), speech errors–sibilants (Karlsson, Shriberg,

Flipsen, & McSweeney, 2002), and speech errors–rhotics (Shriberg, Flipsen, Karlsson, & McSweeney, 2001). Several studies in progress address diagnostic markers for SD-DYS, a subclinical speech motor control disorder possibly associated with what some researchers consider to be a recent trend toward overdiagnosis of SD-AOS (cf. Davis, Jakielski, & Marquardt, 1998; Shriberg & Campbell, 2003; Shriberg & McSweeney, 2002).

## Summary and Statement of the Problem

Although diagnostic markers have been proposed to identify and quantify language impairment (e.g., Bortolini, Caselli, Deevy, & Leonard, 2002; Conti-Ramsden & Botting, 2001; Rice & Wexler, 1996; Tager-Flusberg & Cooper, 1999), to our knowledge there are no studies to date that have reported a perceptual- or acoustic-based diagnostic marker specific for children who may have increased genetic load for speech delay. Rather, the speech genetics literature has used either case records data or direct assessment, including testing on endophenotypes such as phonological awareness, working phonological memory, and speed of processing, to classify the speech status of probands and especially family members. The present study posed two questions: Is there a speech error or error pattern that meets diagnostic accuracy criteria for a potential phenotype marker for SD-GEN? And if such an error pattern is identified, is there any support for viewing it as at least consistent with a constraint in cognitive-linguistic processing?

## Method

### Description of Participants

Participants were selected from an archive of several hundred audio-recorded conversational speech samples from children meeting criteria for USD, as previously defined. The samples had been obtained for cross-sectional and longitudinal research projects conducted locally and with investigators at two other research sites during the current and past decade. Narrow phonetic transcription and prosody-voice coding of these samples had been completed following procedures developed for research in typical and atypical speech development. Transcriptions and prosody-voice codes, as well as the associated assessment and case history information described below, had been entered into a database and processed by a software suite for research in childhood speech sound development (Shriberg, Allen, et al., 2001).

Table 2 is a summary of demographic and speech-language information for the 72 participants who met selection criteria for the present study. Inclusionary criteria required that children (a) have active speech delay of unknown origin (i.e., not associated with known cognitive, sensory, structural, motor, or affective disorder), (b) have been assessed on formal or informal protocols that classified their current language status, and (c) have completed a family pedigree questionnaire for speech-language and other developmental

disorders. As described below, the primary independent variable in the present study was family history for speech delay. Participants in Group 1 had two or more nuclear family members with current or prior speech-language impairment. This criterion was purposefully more conservative than the conventional criterion of one affected member used in familial aggregation studies. Such participants are classified as belonging to *multiplex* nuclear families, in which there may be increased genetic load for the disorder (although typically for binary disorders rather than for quantitative traits). Participants in Group 2 had no affected members. Such participants are classified as belonging to *simplex* nuclear families in which inferably there may be reduced genetic load for the disorder. More specific measures of genetic load (i.e., kinship coefficients; see, e.g., Wijsman et al., 2004) could not be computed for each family member due to incomplete, direct assessment information on nuclear family members in the data sets used in this study. Thus, potentially confounding variables such as family size were uncontrolled using the present simple additive method (i.e., counts of affected family members). Customary (asymptotic) *t* tests, chi-square tests, exact significance tests, and effect sizes were computed for each pairwise comparison. For each of the six independent variables in Table 2, there were no statistically significant differences at the .05 level or greater on any comparison (the largest effect size was 0.328).

**Table 2.** Descriptive statistics for two participant groups with speech delay divided by familial aggregation status.

		Group 1 (n = 24)		Group 2 (n = 48)		Total (n = 72)	
		n	%	n	%	n	%
Age (years;months)	M	5;0		4;8		4;9	
	SD	1;3		1;1		1;2	
Gender	Male	15	62.5	35	72.9	50	69.4
	Female	9	37.5	13	27.1	22	30.6
Source	Iowa	5	20.8	9	18.8	14	19.4
	Ohio	10	41.7	18	37.5	28	38.9
	Wisconsin	9	37.5	21	43.8	30	41.7
PCC	M	70.0		71.6		71.0	
	SD	10.3		10.2		10.2	
Language	Typical	7	29.2	15	31.3	22	30.6
	Questionable <sup>a</sup>	2	8.3	9	18.8	11	15.3
	Impaired	15	62.5	23	47.9	38	52.8
	Missing data	0	0.0	1	2.1	1	1.4
OME	Negative	6	25.0	15	31.3	30	29.2
	Questionable	11	45.8	19	39.6	52	41.7
	Positive	2	8.3	3	6.3	10	6.9
	Missing data	5	20.8	11	22.9	29	22.2

<sup>a</sup>The data from Iowa and Ohio were divided into *typical* versus *delayed*. The three-way classification, including *questionable*, was used only within the Madison data. PCC = Percentage of Consonants Correct; OME = otitis media with effusion.

*Age and gender.* Participants were predominantly preschool age, with an overall mean age for the two groups of 4;9 (years;months;  $SD = 1;2$ ). Approximately 69% of the children were males. The overall male-to-female ratio of approximately 2.3:1 agrees with the average ratio of 2.3:1 reported in several preschool-age clinical referral samples (Shriberg & Kwiatkowski, 1994) but is higher than the 1.5:1 ratio of speech-delayed boys and girls found in an epidemiologically well-defined population sample of 6-year-old children (Shriberg et al., 1999).

*Source.* The speech samples were obtained from children living in three U.S. cities, including 28 children from the Cleveland, OH, area; 14 from a tri-city area in Iowa; and 30 from the Madison, WI, area. The speech samples obtained from Iowa included children from urban, suburban, and rural social strata, whereas the samples from Cleveland and Madison were primarily from urban and suburban strata. A total of 88.9% of the children were Caucasian, and 9.7% were African American, with 1 child's background crossing several categories.

*Speech competence.* The average speech competence of participants in the two groups, as assessed by their scores on the Percentage of Consonants Correct (PCC) metric (Shriberg, Austin, Lewis, McSweeney, & Wilson, 1997a), was 71.0% ( $SD = 10.2\%$ ), which is consistent with a mild-moderate level of severity and similar to findings reported for a large sample of children with USD (Shriberg & Kwiatkowski, 1994). Of central importance to the present findings, the average PCC scores for participants in the two groups were within 1.6 percentage points of one another, as shown in Table 2.

*Language status and otitis media history.* For Iowa and Cleveland participants, classification of language as typical or impaired was accomplished using the Test of Language Development—Primary, Second Edition (TOLD-P:2; Newcomer & Hammill, 1988) and criteria described in Tomblin, Records, and Zhang (1996). For Madison participants, a two-part procedure was used to classify children's language using a three-level ordinal classification system (*typical, questionable, or impaired*). Classification of participants into one of these three classes was accomplished by a clinical instructor supervising students who treated Madison participants during at least one semester at a university clinic. As part of their practicum responsibilities, students had administered one or more of the following language measures to their clients: The Peabody Picture Vocabulary Test—Revised (Dunn & Dunn, 1981), one or more subtests from the TOLD-P:2 (Newcomer & Hammill, 1988), and one or more subtests from the Clinical Evaluation of Language Fundamentals—Revised (Semel, Wiig, Secord, & Sabers, 1987). Additionally, for some children, the clinical supervisor had

completed a structural stage analysis (Miller, 1981) based on one or more language samples. The clinical instructor used a series of conservative conversion criteria (e.g., percentile scores above the 16th percentile were classified as within the typical range), supplemented by additional language data obtained during the semester, to classify the children's language status using the three-level ordinal system.

As indicated in Table 2, approximately 53% of the participants in this study had comorbid language impairment, with another approximately 15% considered questionable for language impairment. These figures are consistent with speech-language delay comorbidity figures for children of this age summarized from several studies (Shriberg & Austin, 1998).

Participants' OME/hearing loss status (*negative, questionable, or positive*) in all three sites was classified using available case history information on the number of OME episodes, audiological results, parents' comments about their children's hearing, and/or possible insertion of pressure equalization tubes. The amount of usable information varied. Participants were classified as positive for hearing loss if they had failed a hearing screening and/or had had tubes inserted. They were coded as questionable for hearing loss if they had had at least four episodes of OME. This later criterion was used to accommodate the varied criteria that classify children as having positive (i.e., meets criteria for OME/hearing loss) versus negative histories of OME/hearing loss. Criteria for a positive history using clinical data have ranged from approximately three to approximately six episodes of unilateral or bilateral OME (cf. Roberts & Hunter, 2002) during the first 3 years of life. Children with significant histories of OME had been screened out of the study conducted at the Cleveland site. As shown in Table 2, using these conservative inclusionary criteria, only 6.9% of participants in the two groups (i.e., those meeting the otological and/or audiological criteria for positive) had histories that clearly placed a child at auditory-perceptual risk for speech delay.

The summary data in Table 2 and findings from the inferential statistical comparisons are proposed as support for viewing participants in the two groups as having comparable histories and status on sociodemographic, speech-language, and middle ear variables. Moreover, the data on this sample of participants with speech delay are viewed as consistent with extant speech and language descriptions of this clinical population.

## **Familial Aggregation**

The procedures used to classify children's nuclear biological family members as affected for speech-language

disorders varied for the samples obtained at the three sites. A telephone interview with a caregiver provided the data for the Iowa site. The other two sites used information from a family history questionnaire completed by one or both parents of a child identified by a local clinician as having a significant speech intelligibility problem. Family history questionnaires differed from one another in formats, but each provided comparable information on the types of verbal trait disorders (i.e., speech, language, reading, spelling, and learning disorders) that the proband and family members were currently experiencing or had experienced. For participants from the Cleveland and Madison sites, a family member was classified as affected if he or she currently or previously had a speech disorder with or without a language disorder. For the Iowa site, a family member was classified as affected if he or she had a speech and/or language disorder.

In cases where two probands in the same family were known to be monozygotic twins, only one was randomly selected for the pedigree analysis. If probands were dizygotic twins (or nontwin siblings), both were included in the pedigree analysis. Monozygotic twin siblings of probands were counted as one sibling, and dizygotic twin siblings as two siblings. Immediate family members under age 4 whose speech-language status had not been directly evaluated were not included in family member counts unless they were or had been enrolled in speech-language therapy. Similarly, siblings younger than age 8 were not included in counts for associated longer term verbal trait disorders unless they reportedly had received special instruction or tutoring in these areas.

The relatively modest size of the present sample prohibits information on the kinship positions of affected family members, which are typically stratified by family size. Total family sizes were not available for the Iowa data set, in which the telephone interview procedure provided incomplete data on the number of affected and nonaffected siblings. Thus, the available family size information at the time of ascertainment was limited to 19 (79%) of the Group 1 participants and 38 (79%) of the Group 2 participants. One proband in Group 2 had four siblings, and all others in both groups had no more than three siblings. For this subsample there was a significant trend ( $t = 4.11, p = .0003$ ) for probands in Group 1 to have more siblings ( $M = 2.0, SD = 1.11$ ) than probands in Group 2 ( $M = 0.80, SD = 0.92$ ). However, the 95% confidence interval for the differences in means was large (0.61–1.8). Most generally, the familial aggregation data obtained for Group 1 included all combinations of affected kinship positions (i.e., two parents, two siblings, or one parent and one sibling), with proportionally more affected brothers

than sisters but equivalent proportions of affected fathers and mothers.

## **Perceptual Measures, Analyses, and Reliability**

The conversational speech samples from participants at the three study sites were obtained using similar or comparable recording equipment, recording techniques, and speech sampling guidelines. Each sample consisted of an examiner talking with a child about favorite home and school activities and recent events. For some children, pictures were used to suggest topics. Examiners verbally glossed speech that was likely to be unintelligible to transcribers, following a protocol that was minimally intrusive on natural discourse (i.e., glossing was explained to the child as having the authentic goal of “understanding the child’s ideas” and was timed not to interrupt).

Transcription and prosody-voice coding of each sample was completed by one of five research transcribers using a set of narrow phonetic transcription symbols and transcription formatting conventions developed for research in child SSDs (Shriberg, Allen, et al., 2001). These transcriptions occurred within a larger study that included 121 children whose demographics and speech characteristics were similar to those shown in Table 2. Each of the five transcribers had completed transcriptions for at least 1 and as many as 20 of the participants in the two groups.

An interjudge reliability assessment was obtained that included 12 randomly selected conversational samples. A utility in the software suite was used to complete 20 interjudge agreement comparisons, including 12 two-transcriber comparisons for 8 of the 12 samples and 8 three-transcriber comparisons on the remaining 4 samples. The point-to-point percentages of agreement were as follows: narrow agreement consonants ( $M = 73.9, SD = 4.5$ ), narrow agreement vowels ( $M = 73.8, SD = 6.8$ ), broad agreement consonants ( $M = 89.3, SD = 3.0$ ), and broad agreement vowels ( $M = 86.3, SD = 4.0$ ). These percentages are within the agreement ranges reported in other studies of speech delay (Shriberg & Lof, 1991) and were considered adequate for the data to be reported.

## **Acoustic Measures, Analyses, and Reliability**

A subgroup of the speech samples was selected for acoustic studies to characterize the participants’ sibilant distortions, information that has been useful in diagnostic marker studies for SSDs referenced previously. A lexical search of the transcripts yielded a list

of 18 commonly occurring words that included at least one of the sibilants /s/, /z/, and/or /ʃ/ in primarily monosyllabic words. Ten of the words had /s/ in the word-initial or word-final position, 6 with /z/ in word-final position, and 2 with /ʃ/ in word-initial position. To be eligible for the subgroup analysis, a participant had to have produced at least 5 of these words in which the sibilant was judged perceptually correct, was transcribed using any diacritic modification, or was transcribed as having substitution of another fricative for the target sibilant (i.e., sibilant deletions or out-of-manner substitutions were not eligible). A total of 12 children from Group 1 and 13 children from Group 2 contributed at least 5 but not more than 10 tokens to the final acoustic sample of 153 sibilant tokens (74 from Group 1, 79 from Group 2). Each of the 25 participants contributed tokens for at least two different sibilants and at least two different word positions. These procedures yielded a final set of 13 words, including 5 with word-initial /s/ (*see, say, some, so, saw*), 3 with word-final /s/ (*this, yes, house*), 4 with word-final /z/, (*is, was, those, because [cause]*), and 1 with word-initial /ʃ/ (*she/she's*). The number of tokens per word ranged from 4 to 24, with approximately equal number of tokens from children in each group.

All words were digitized at a 20-kHz sampling rate, using a Kay Elemetrics CSL 4300B system fed by a Tascam 112MKII tape deck. Segmentation of the sibilants within each word was accomplished in the TF32 (Milenkovic, 1996) environment, followed by moments analyses. Based on previous studies of sibilant errors in children with typical and atypical speech acquisition (Flipsen, Shriberg, Weismer, Karlsson, & McSweeney, 1999), the spectral energy data quantified as Moment 1 were obtained on the temporal middle 20 ms of the sibilant spectra. Additional details on segmenting and analysis procedures, as well as reference data for these analyses, are available in Flipsen et al. (1999).

Interjudge and intrajudge reliability estimates were obtained for the acoustic data. One of the original two assistants resegmented a randomly selected 15 tokens for an approximately 10% intrajudge agreement estimate, and a highly experienced judge (fifth author) resegmented 19 tokens for an approximately 12% interjudge agreement estimate. As there were no directional trends observed in either set of remeasurements, agreement was expressed as the absolute value of the original compared with remeasured M1 values (in kHz). Both the intrajudge ( $M = .2667$ ,  $SD = .2703$ ) and interjudge ( $M = .2238$ ,  $SD = .2180$ ) differences in M1 values were consistent with acoustic reliability data for sibilant productions in the studies cited above and were considered adequate for the data to be reported.

## Results

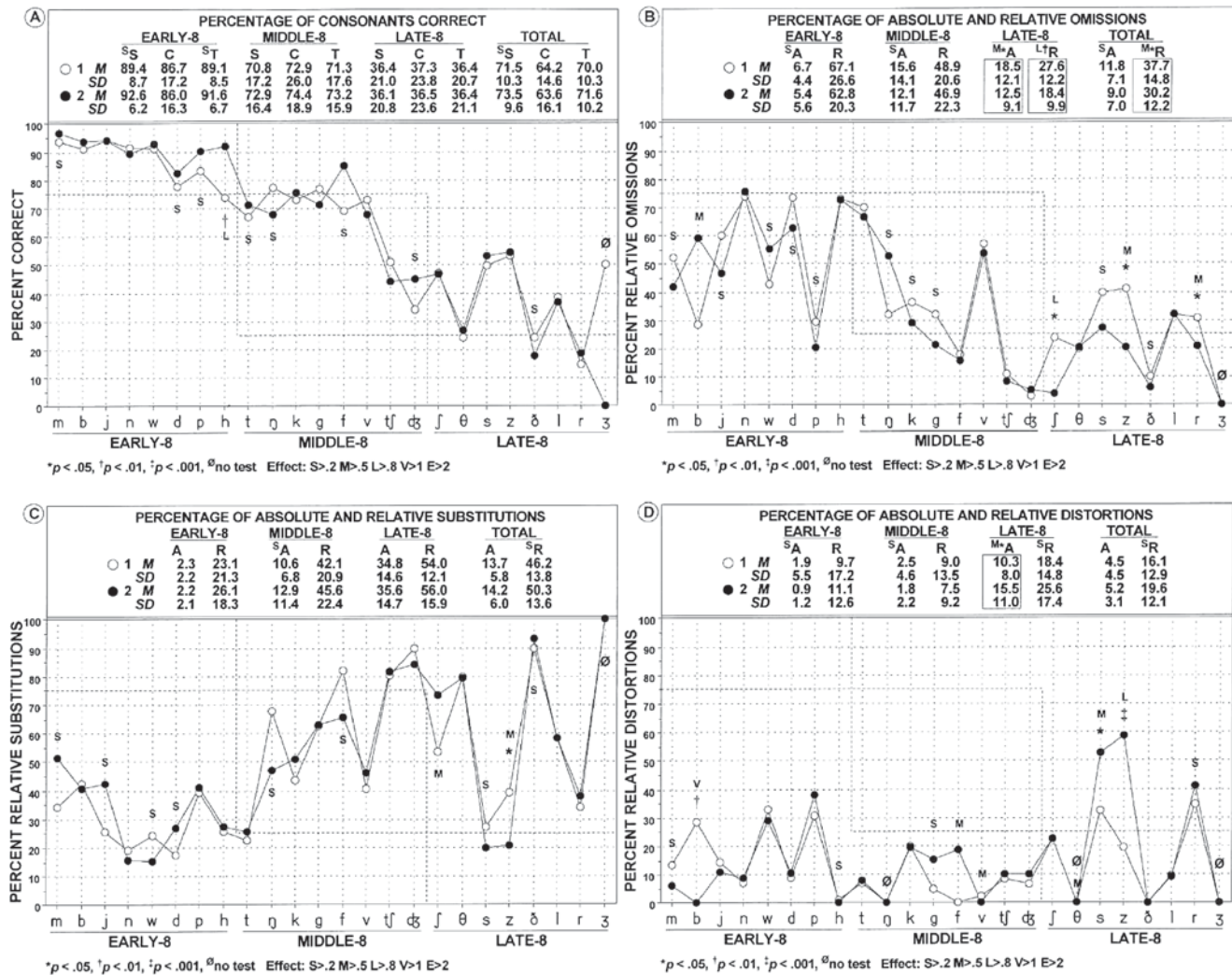
### Perceptual Findings

Figure 2 provides the perceptually based data toward a set of diagnostic and phenotype markers for SD-GEN. Supplemental statistical information for each variable (i.e., cell size, skew, kurtosis, confidence intervals) was used to interpret and constrain generalizations from the descriptive statistics shown for each speech variable in Figure 2.

*Group 1 and Group 2 children had similar distributions of correctly articulated consonants.* The top left panel (Panel A) in Figure 2 includes numerical information (top section) on the PCC scores for participants in Group 1 (means and standard deviations in the first two rows) and Group 2 (second two rows). PCC data percentages are provided for singleton (S), cluster (C), and total (T) targets for the 24 English consonants, divided into three categories termed *developmental sound classes* (i.e., the Early-8 sounds, Middle-8 sounds, and Late-8 sounds; Shriberg, 1993) and totaled across the three classes (the metric shown in Table 1). The graphic section on the bottom of Panel A provides PCC scores for each of the 24 consonants, sequenced left to right by the three developmental sound classes. Given the large number of analyses described previously, the only comparisons considered relevant for the theoretical and applied goals of the present study were those with at least medium effect sizes ( $>0.50$ ) that clustered in conceptually coherent patterns.

The two groups' profiles of correctly articulated speech sounds did not differ significantly from one another, nor were they associated with at least medium effect sizes (other than one significant statistical finding and associated large effect size for percentage of correct /h/ targets). Notice in the numerical section that the means and standard deviations for each of the three developmental classes were essentially similar for the two participant groups, with both groups averaging approximately 90% correct for the Early-8 consonants, approximately 72% correct for the Middle-8 consonants, approximately 36% correct for the Late-8 consonants, and approximately 71% correct across all consonants (see also Table 2). Several comparisons yielded small effect sizes (0.20–0.49 *SD* units; Cohen, 1988). As above, isolated statistically significant findings were not unexpected, due to the large number of statistical comparisons performed on these and associated comparisons. Thus, the profiles of correctly articulated speech sounds of children with possibly increased (Group 1) and decreased (Group 2) genetic load for speech delay were considered to be essentially similar. Comparable findings were

**Figure 2.** Perceptual findings for children with speech delay from immediate families with high (Group 1) versus low (Group 2) familial aggregation of speech-language disorders. The open circles are the data for Group 1 and the filled circles for Group 2. The abbreviations are as follows: S = singleton; C = cluster; T = total of singletons and clusters; A = absolute percentage; R = relative percentage. Note that the graphic data in Panels B, C, and D are relative error percentages. Statistically significant comparisons are indicated by the conventional symbols and by a box in the numeric panel. Effect size abbreviations, as indicated at the bottom of each panel, are as follows: S = small; M = medium; L = large; V = very large; E = extremely large.



obtained for the prosody-voice analyses, with only small effect sizes for between-group comparisons and no coherent pattern to the few statistically significant differences.

Group 1 participants' speech errors were more frequently omissions. The remaining three panels in Figure 2 provide descriptive and inferential statistical information on the error profiles of children in Groups 1 and 2. Panel B provides information on the distribution of errors classified perceptually as omissions, Panel C on substitutions, and Panel D on distortions. The general format of each panel is similar to the format described for Panel A, but error percentages are reported in two ways. For each of the three devel-

opmental sound classes (and as totaled [T] across the three classes), the absolute (A) error percentages for each child are based on the number of all attempted targets for that class. That is, the numerator is the total number of incorrect targets meeting the definition for that error type, and the denominator is the sum of a child's attempted targets for that category. In contrast, the relative (R) percentages use the same numerator, but the denominator is the sum of all incorrect attempts at that target (i.e., the sum of all omissions, substitutions, and/or distortions). Thus, relative percentages of each error type control for overall severity of involvement. For example, if a child made 10 omission errors on 100 phonemes, these errors yield

an absolute omission error percentage of 10%. But if those were the only errors she made on the 100 phonemes, her relative omission error percentage would be 100%. If she made 10 omission errors, 10 substitution errors, and 10 distortion errors her relative omission errors would be 33.3% (as would be her relative substitution errors and relative distortion errors). Note that the graphic data in the lower section of each panel provide the relative error percentages, between-group statistical comparisons, and effect sizes for the individual 24 consonants, as subgrouped within the three developmental sound classes.

The data in the numeric and graphic sections of Panel B indicate that, in contrast to participants in Group 2, the speech errors of participants in Group 1 were significantly more often speech sound omissions. Statistically significant findings were obtained for three of the comparisons in the numeric panel (absolute and relative omissions of Late-8 consonants and relative omissions of all consonants), as well as for three of the Late-8 consonants (*/j/*, */z/*, and */r/*) in the graphic section. Effect sizes for these significant comparisons ranged from medium to large (0.50–0.99). Descriptively, a trend for Group 1 participants to average more omission error types than Group 2 participants was observed on all of the eight comparisons in the numeric section of Panel B, and on 16 of 23 (approximately 70%) of the individual relative percentage comparisons for the consonant speech sounds in the graphic section.

*Group 1 and Group 2 participants had equivalent proportions and types of substitution errors.* As indicated in Panel C in Figure 2, the proportion of substitution errors was essentially similar for participants in Groups 1 and 2. There were no statistically significant differences and no effect sizes at the medium level or above for the comparisons summarized in the numeric panel. The relative percentages of substitution comparisons for individual sounds yielded two Late-8 comparisons with medium effect sizes (*/j/*, */z/*). However these findings were not consistent in direction, as indicated by the interleaving pattern of differences across the 23 consonant comparisons.

*Group 1 participants' speech errors on Late-8 consonants were less frequently distortions.* The fourth finding toward diagnostic and phenotype markers for SD-GEN is that the Late-8 consonant errors of Group 1 participants were less often distortions (Panel D), in comparison with those of Group 2 participants. Statistically significant findings for this trend were obtained for the absolute percentage of Late-8 distortions, with the source of this effect clearly due to Group 1 participants' low proportion of relative */s/* and */z/* distortions (associated with medium and large effect sizes, respectively). As shown in the graphic section of Panel D,

Group 1 participants also had a significantly higher percentage of relative distortion errors on */b/*, but this finding is not considered empirically robust because, as shown in Panel A, participants in both groups misarticulated less than 10% of */b/* targets.

## Acoustic Findings

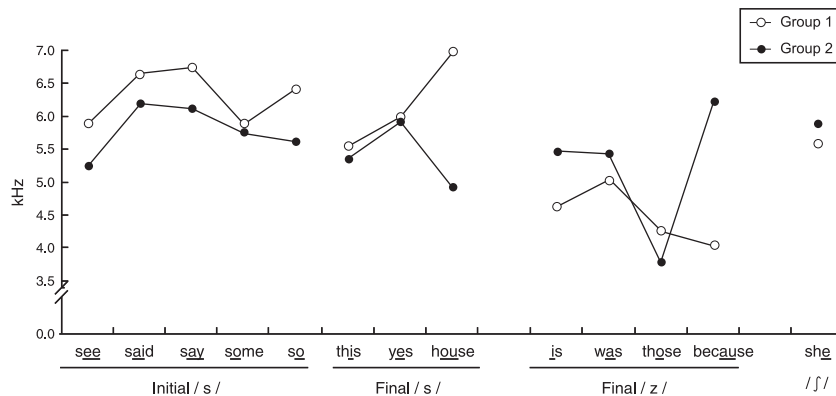
Two acoustic analyses were completed to cross-validate the auditory perceptual (i.e., transcription) findings and to provide information that might contribute to potential explanatory origins of a diagnostic marker for SD-GEN.

*Acoustic analyses of /s/ and other sibilants.* As described above, spectral moments analyses were completed on 13 word types sampled from the conversational speech of Group 1 and Group 2 participants. Each word token contained either a perceptually correct sibilant, a diacritic-level distortion of one of the three sibilants, or in a few instances, a within-class sibilant substitution. The data of particular interest were the 8 words that included */s/* in either word-initial (*see, said, say, some, so*) or word-final (*this, yes, house*) positions. Previous research on speech markers for SD-OME (Shriberg, Kent, et al., 2003) has indicated that a significant number of children with positive histories for SD-OME had */s/* distortions perceived as *backed* by research transcribers. Acoustically, such distortions had lowered first spectral moments (M1). The present question was whether the */s/* distortions obtained from participants in Group 1 (who may have had increased genetic load for speech delay) would have higher M1 values (i.e., nonbacked) relative to those obtained from participants in Group 2.

Figure 3 is a graph of the average M1 values for tokens of the eight */s/* words obtained from the conversational speech samples. For comparison, the data from the five words with */z/* and the one word with */j/* are also shown. For each of the eight comparisons of the */s/* distortions, the average M1 value for participants in Group 1 was higher than for participants in Group 2 (test of proportions:  $p = .008$ ). However, effect sizes were negligible to small for seven of the comparisons; as shown in Figure 3, there was a large (0.81) effect size for the M1 comparison for *house*.

The acoustic data for the productions of */z/* and */j/* were not consistent with the M1 data for */s/* productions. The average M1 values for four of the five comparisons on these latter two sibilants were lower for Group 1 participants, with the comparison for */z/* in *because/cause* associated with a medium (0.55) effect size. Methodological implications of these data toward development of a diagnostic marker for SD-GEN are considered in later discussion. For the present

**Figure 3.** Acoustic support for the percept of more frequent backing of /s/ in children with speech delay from nuclear families with reportedly no familial aggregation of speech-language disorders (Group 2). The data points are average values for the first spectral moment (M1).



methodological focus, the data for /s/ in Figure 3 are viewed as providing construct validity for the transcribers' auditory percept of fewer backed /s/ distortions in Group 1 participants.

### **A Preliminary Diagnostic/Phenotype Marker for Genetically Transmitted Speech Delay**

Machine learning routines (Kiselev, Arseniev, & Flerov, 1994) were used to classify Group 1 and Group 2 participants, using the speech data from the output shown in Figure 2 and from outputs that yielded information on 156 of the perceptual speech variables. These perceptual variables provided articulatory detail (similar to that in Figure 1) for vowels/diphthongs; for phonemes at the level of place, manner, and voicing features; and for a set of clinical and nonclinical distortion types (i.e., as narrowly transcribed using the diacritic system described in Shriberg & Kent, 2003). The acoustic data supporting the perceptual findings for sibilant distortions were not used in the machine learning routines. Recall that the error data in Panels B, C, and D (Figure 2) indicated that the differences between the two study groups were in the proportions of omission versus distortion errors on Late-8 consonants, particularly on /s/ and /z/. Previous research on sibilant errors had led to the development of database values that divide children's sibilant distortions into *dentalized* or *fronted* versus *backed*. The software classified sibilants as backed if they had been transcribed using the diacritics for *palatalized* or *retroflexed*. Also, because prior reliability data indicated unstable agreement for substitutions of /ʃ/ for /s/ (i.e., vs. backed /s/), the software also tallied occurrences of these substitutions as backing. Inspection of these data indicated

that Group 1 participants averaged 3.0 ( $SD = 3.8$ , range = 0–14) backed sibilants per speech sample, whereas Group 2 participants averaged 7.8 ( $SD = 15.8$ , range = 0–96) backed sibilants per sample. Using a conservative criterion of 4 or more backed tokens to classify a participant as having backed sibilants, 2 (12.5%) Group 1 participants were so classified, compared with 20 (41.7%) Group 2 participants.

Inspection of the distributions of backing scores for each group, as well as of group scores on variables expressing the ratio of omissions to distortions, indicated severe departures from normality. To meet normality assumptions for the machine learning analyses, Poisson transformations were applied to 156 speech variables, including 15 values reflecting the ratios of participants' omissions to distortions (i.e., by total sounds, developmental sound class, manner feature, and error type on individual sibilants).

The Appendix includes the machine learning classification rule that yielded the maximum classification accuracy using the perceptual speech error data. As indicated in the footnote to the Appendix, the classification rule required values for each of the terms, thereby eliminating classification outcomes for two participants in Group 2 (the software had given them missing value codes for backed /s/ distortions, because they had no /s/ distortions to use as the denominator). The classification rule can be parsed as follows: if the reciprocal of a participant's ratio of relative Late-8 omission errors to backed /s/ errors plus a constant (6.42) was greater than 0.000103, AND if this same value was less than 0.000103 plus the product of a constant (0.073) times the participant's ratio of relative Late-8 omission errors to their relative Late-8 distortion errors, THEN classify the participant as Group 1; ELSE classify the participant as Group 2. Notice that the primary speech measures in this rule—the

relative omission index for the Late-8 consonants (ROI\_Late-8)—is consistent with the significant groupwise difference on this variable shown in Figure 2. The second rule addressing Late-8 distortions—the relative distortion index (RDI\_Late-8)—is somewhat consistent with the findings in Figure 2, which indicate a significant pairwise difference only for the absolute distortion index. Substantive aspects of the findings for the third term in the rule, backed /s/ errors, are addressed below.

The second and third sections in the Appendix provide the classification outcomes for the rule. Sensitivity of the classification rule was not high, with only 15 of 24 participants in Group 1 correctly classified by the rule. However, the positive predictive values indicate that 83% of persons who were classified as positive by the rule/marker may have had increased genetic load for speech delay (Group 1), whereas the 83% classified as negative may have had decreased genetic load for speech delay (Group 2). Also, the positive and negative likelihood ratios, respectively, approach the 10:1 and <.20 values desired for those two diagnostic accuracy variables (Sackett, Haynes, Guyatt, & Tugwell, 1991). These diagnostic accuracy findings are viewed as promising, pending further refinement of the classification rule and crossvalidation of the rule using larger, more demographically diverse samples.

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## Discussion

The primary question posed in this study was whether there may be a diagnostic marker for a proposed genetically transmitted subtype of childhood SSD. A secondary question is whether the marker is consistent with current findings indicating that some type of cognitive-linguistic processing deficit underlies the speech-language deficits that have been reported in linguistic genetic studies. The following discussions consider methodological and substantive issues for each of these questions.

### Methodological Needs

The first methodological need is to refine the independent variable indexing risk for genetically based speech delay, which in the present study was a preliminary metric based on participants' familial aggregation status. As reviewed previously, the rationale for this approach is based on two findings: the many familial aggregation studies documenting higher prevalence rates of speech-language delay in families of probands compared with control families (cf. Stromswold, 1998) and the finding in the sociodemographically di-

verse study reported by Campbell et al. (2003) that familial aggregation was one of three risk factors significantly associated with speech delay. The latter article used the speech classification system described in the present report. As discussed previously, however, we are keenly aware of both the methodological and conceptual limitations of familial aggregation as a proxy for genetic load and the limitations in applying this construct to quantitative traits. None of the studies reviewed previously have documented that the sheer number of family members positive for lifetime affection status provides a metric indicating that, for example, children with no affected family members are *not* at genetic risk for speech delay. A collaborative familial aggregation study currently in process addresses the need for information on the gender, kinship position, and family size of probands with speech delay and well-matched case controls.

The second major methodological need is to improve the diagnostic accuracy of the decision rule identified in this study. Increased diagnostic accuracy is expected to be gained by increasing specificity in two ways—by using larger sample sizes with kinship coefficients available for each family and by using exclusionary criteria based on diagnostic marker information on the other putative subtypes of SSDs shown in Figure 1. As discussed in the next section, the primary alternative etiological subtype is associated with middle ear disease.

A third methodological need is to increase the sensitivity and specificity of the perceptual data. The present spectral mean findings for /s/ but not for /z/ suggest that there are coarticulatory and other well-studied articulatory processes that can be exploited to improve the sensitivity of the perceptually based backing term in the classification rule shown in the Appendix. As shown in Figure 3, the largest between-group M1 differences in /s/ production for Groups 1 and 2 occurred in *house* and *so*, contexts in which /s/ was preceded or followed by diphthongs made in the back of the mouth. In contrast, the smallest between-group differences in M1 occurred on /s/ in *some*, *this*, and *yes*, contexts in which /s/ is adjacent to more anterior or mid vowels.

Finally, the reliability and efficiency of phonetic transcription are problematic, especially when behaviors at the subphonemic level require accurate measurement. The acoustic findings in Figure 3 indicate the potential contributions of acoustics and acoustic-aided phonetic transcription to identify valid and reliable segmental and suprasegmental markers. A long-term goal especially for clinical use of diagnostic markers is to implement automatic speech recognition systems for these tasks (e.g., Hosom, Shriberg, & Green, 2004).

## Support for a Cognitive-Linguistic Processing Constraint in SD-GEN

The present findings of increased omission errors and fewer backed-type /s/ distortions in Group 1 participants are viewed as consistent with contemporary findings suggesting that a cognitive-linguistic processing constraint underlies some genetically transmitted verbal trait disorders. The following three perspectives on omissions and distortions of phonemes in manifest speech are proposed as support for the coherence of these errors as a potential diagnostic marker for SD-GEN.

*Omission errors are consistent with a cognitive-linguistic processing delay.* The first term in the two-part classification rule in the Appendix indicated that Group 1 participants had proportionally more relative omission errors on Late-8 consonants. In contrast to substitution and distortion errors, increased omission of challenging speech sounds has both construct and concurrent validity as reflecting a cognitive-linguistic constraint. Whereas substitutions (particularly within-class) and distortions indicate at least partial underlying knowledge of the target phoneme, phoneme deletions may indicate lack of phonological representation of targets (i.e., to encode, store, and/or successfully retrieve them). Empirically, disproportionately high rates of omission-type speech errors have been reported as speech-error pattern correlates of intellectual deficits (see discussion of a cognitive capacity constraint in Shriberg & Widder, 1990).

Omission errors also have concurrent validity as an index of phonological competence within the present data. First-order correlation coefficients of the combined sample of 72 participants with speech delay were computed for the association of PCC, the measure of speech competence, with each of the three error type indices shown in Figure 2—ROI, relative substitution index (RSI), and RDI. ROI had the expected and significant negative correlation with PCC ( $r = -.359$ ,  $p < .002$ ,  $r^2 = 12.9\%$  common variance), whereas RSI was uncorrelated with PCC ( $r = .081$ ,  $p = .497$ ,  $r^2 = <1\%$  common variance), and RDI was positively correlated with PCC ( $r = .302$ ,  $p = .010$ ,  $r^2 = <9.12\%$  common variance). Thus, ROI was the severity-adjusted, error-type metric that was most closely associated with participants' severity of delay as sampled in conversational speech.

*Few backed distortions are consistent with a cognitive-linguistic processing delay.* The classification rule shown in the Appendix also indicates that when Group 1 participants distorted /s/ sounds, the distortions were typically fronted, that is, less often backed. Findings from several studies can be marshaled to

support a cognitive-linguistic delay as the proximal processing constraint underlying these findings.

First, fronting of sibilants was found to be the most frequent type of sibilant distortion (primarily dentalized /s/ and /z/) in two studies using similar measurement procedures—Lewis and Shriberg (1994), in a study of adult family members of children with USD, and Karlsson et al. (2002), in a study of adolescents with histories of USD and speech errors. In contrast, backing of sibilants was observed significantly more often in children with speech delay who had histories of frequent early recurrent OME (Shriberg, Kent, et al., 2003). As shown in Figure 1, Level II, we posit an auditory-perceptual processing deficit associated with fluctuant hearing loss as the proximal explanatory source for such speech sound differences (see Whitehill, Francis, & Ching, 2003, for a similar perspective on posterior placement of speech sounds in children with cleft palate). A technical report using acoustic methods supported the perceptually based data in Karlsson, Shriberg, Scheer, and Nadler (2003); acoustic support was also provided for the backing findings in the present article (Figure 3).

Unfortunately, the present data do not allow for a direct test of the hypothesis that increased backing in Group 2 participants was associated with histories of significant hearing loss. OME can occur with or without hearing loss, and although parent-reported data on episodes of OME were available for some participants (Table 2), reliable information on their hearing status throughout the speech acquisition period was not available. Approximately 30% of children referred to a university speech clinic for speech delay of unknown origin are estimated to have a positive history of OME, as defined by a cluster of otological and audiological variables (Shriberg & Kwiatkowski, 1994). Thus, it is plausible that the origin of the speech delay in Group 2 participants—children who had both no affected family members and more frequently backed /s/ distortions—was a deficit in auditory-perceptual rather than cognitive-linguistic processing, particularly for those from the Madison site (i.e., participants in the Cleveland and Iowa sites were recruited for studies, rather than clinically referred).

To summarize, whereas the fronted /s/ distortions in Group 1 are proposed to reflect the phonetic and phonologically natural consequences of delays in a genetically transmitted cognitive-linguistic deficit, the more frequently backed /s/ distortions in Group 2 participants may reflect delays primarily due to genetic and environmentally based risk factors associated with middle ear disease. The latter distal risk factor—fluctuant hearing loss associated with early frequent OME—is posited to affect the auditory-perceptual

processing of speech forms, in turn affecting the fricative spectra for sibilant productions.

*Trends in language status and scores on a nonsense word repetition task were consistent with a cognitive-linguistic processing delay.* The final proposed support for a cognitive-linguistic processing deficit component underlying the speech delay in Group 1 participants considers some limited data on participants' language status and their scores on a nonword repetition task. As shown in Table 2, there was a nonsignificant trend for more of the children in Group 1 to have comorbid language impairment (Group 1 = 62.5%, Group 2 = 47.9%), as classified using a three-category ordinal system. This preliminary finding, if reliable, is consistent with the hypothesis of greater cognitive-linguistic involvement for Group 1 participants.

Additional, albeit limited, information based on scores on the Nonword Repetition Task (NRT; Dollaghan & Campbell, 1998) was available for children tested at the Iowa research site, including 5 participants from Group 1 and 9 participants from Group 2. The task had been administered using the standard audio stimulus tape (Ellis Weismer et al., 2000). One of the attractive features of this task for current purposes was that the stimuli were constructed to exclude sounds that children with speech delay typically misarticulate, specifically the Late-8 consonants (Shriberg, 1993). The NRT includes seven different vowels and diphthongs in the three-syllable words and nine different vowels/diphthongs in the total words, including all five diphthongs. Scores for the one-, two-, three-, and four-syllable words and totals were calculated on three subscales: PCC, Percentage of Vowels Correct (PVC), and Percentage of Phonemes Correct. Preliminary analyses indicated that scores for the three-syllable words and total words were most sensitive to individual differences. Specifically, one- and two-syllable words appeared to be easily repeated correctly (scores on the three metrics averaged 92.6%), and four-syllable words were apparently difficult to repeat correctly (scores averaged 61.5%). Compared with the scores of Group 2 participants, the average nonword repetition scores for Group 1 participants were lower on each of the three metrics for three-syllable words (effect sizes = 0.30–1.12).

These preliminary findings, particularly for the three-syllable PVC metric (Group 1:  $M = 63.4$ ,  $SD = 20.1$ ; Group 2:  $M = 82.4$ ,  $SD = 13.0$ ; effect size = 1.12), are viewed as supporting the possibility of increased cognitive-linguistic constraints in Group 1 participants. The source of the lower scores on repetition of vowels and diphthongs in the NRT would not seem to be due to differences in articulatory constraints. Rather, the source of Group 1's lowered scores on both

vowels/diphthongs and consonants is presumed to reflect constraints in phonological working memory. Whether those cognitive-linguistic influences were in encoding, storage, or retrieval of the consonants and/or vowels/diphthongs—as further influenced by the canonical and individual consonant contexts in each word—cannot be determined (cf. Aguilar-Mediavilla, Sanz-Torrent, & Serra-Raventos, 2002).

## Conclusions

The neurodevelopmental substrates of speech delay include constraints that may be associated with cognitive-linguistic, auditory-perceptual, speech motor, and/or affective processes. The perceptual and acoustic findings in this report are viewed as support for a cognitive-linguistic constraint on the most common subtype of speech delay—that which is posited to be genetically transmitted as a quantitative trait. These appear to be the first data suggesting that such deficits may be identified and quantified in the form of a speech-based diagnostic marker, which may also prove to be useful as a phenotype for probands and family members in speech genetics research. Specifically, children inferred to have increased genetic load for speech delay had a significantly different pattern of errors from those found in control children with speech delay of comparable severity. Cross-validation studies are needed that provide adjustments for family size, that include kinship coefficients to quantify genetic load in simplex and multiplex families, that assess the stability of the machine learning algorithm, and that increase accuracy of the three-part diagnostic marker. Longitudinal studies are needed to assess the stability of the error patterns obtained for the Group 1 participants in the present study during the developmental period. More broadly, as suggested at the outset of this report, an eventual account of the onset, maintenance, and normalization of subtypes of childhood SSDs will require life span measures of genetic and environmental risk and protective factors.

## Acknowledgments

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**Appendix.** Diagnostic accuracy findings for a preliminary phenotype marker of speech delay–genetic.

I. Classification rule<sup>a</sup>

$$\text{If } \frac{1}{\left(\frac{ROI_{Late-8}}{Backed/s/errors}\right) + 6.42} > .000103$$

$$\text{and } \frac{1}{\left(\frac{ROI_{Late-8}}{Backed/s/errors}\right) + 6.42} < .000103 + \left[.073 \times \left(\frac{ROI_{Late-8}}{RDI_{Late-8}}\right)\right]$$

then classify as Group 1;  
else classify as Group 2.

II. Classification outcomes

	Classified by familial aggregation	
	Group 1	Group 2
Classified by rule		
Group 1	15	3
Group 2	9	43
Total	24	46

III. Diagnostic accuracy for the marker

Statistic	Value	95% Confidence Limit
Sensitivity	0.63	0.43–0.82
Specificity	0.94	0.86–1.00
Diagnostic accuracy	0.83	0.74–0.92
Positive predictive value	0.83	0.66–1.00
Negative predictive value	0.83	0.72–0.93
Positive likelihood ratio	9.58	3.07–29.88
Negative likelihood ratio	0.40	0.24–0.68

*Note.* ROI = relative omission index; RDI = relative distortion index.

<sup>a</sup>To be classified by rule, participants must have had a score for each of the three terms in the rule.

## **Toward Diagnostic and Phenotype Markers for Genetically Transmitted Speech Delay**

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