CHAPTER 1

Childhood Speech Sound Disorders: From Postbehaviorism to the Postgenomic Era

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Introduction

Thanks

I'll never forget the sunny spring day in Madison when Rhea and Peter spilled the beans about this book. What an incredible, wonderful surprise. It took two months before I could get my head around the reality of this gracious gesture and hunker down to begin my writing assignment. Rhea and Peter asked me to sketch the "arc" of my research to date. I've tried to capture that rather wobbly line in the title and content of this chapter, and more personally, in the next few paragraphs. I'm sorry there isn't room to thank people individually by name. I trust that each of you will recognize yourself and your influence in the following brief chronology.

My interest in causality research dates back to the masters program in Communicative Disorders at Boston University, where I found an engaging faculty and a terrific group of fellow students with diverse life experiences. After an aimless series of undergraduate majors at Syracuse University, followed by a string of forgettable jobs, BU was a stimulating and challenging experience. We talked in and out of class about the big stuff (e.g., 'the subsoils of human existence'), which somehow set me on a quest to try to understand the origins of speech disorders of unknown origin. The detective work continued at my first clinical position in Bridgeport, Connecticut—a busy rehabilitation center where clients and their families taught me so much more than I helped them.

At the Lawrence and the Medical Center campuses of the University of Kansas,

I had the good fortune to learn "dust-bowl empiricist" research from a scholarly faculty and a knowledgeable, fun-loving, and very verbal gang of doctoral students. The "post-behaviorism" in the chapter title alludes to this heady period in our discipline when carefully planned and reported treatment research offered the possibility to effect significant behavioral and social change. There is much about the earnest goals of the current focus on evidence-based practice that is reminiscent of the Zeitgeist of this period.

At the Department of Communicative Disorders, University of Wisconsin-Madison and the Communication Processes Unit at the Waisman Center, I have been privileged to have long-term interactions with an extraordinary cohort of academic and clinical colleagues and forward-thinking administrators. I want to acknowledge the contributions of dozens of wonderful alumnae from our research group at the Phonology Project, many doctoral and postdoctoral researchers who have shared their skills and enthusiasm with us, and investigators in Madison and elsewhere with whom I have had the honor of working in past and continuing collaborative projects. One long-term collaborator and good friend I will thank by name is Joan Kwiatkowski, who continues to contribute her immense talent to speech research and to set a standard for clinical efficacy in our university and Phonology Project speech clinics. It's such a joy to share with these colleagues the excitement on the other side of the arc—the boundless opportunities for discovery in the current "postgenomic era."

To Rhea, Peter, and each of the other good friends who have written such lucid papers for this volume—and to Sadanand Singh, a long-time friend and tireless advocate for our discipline—my humble and heartfelt thanks.

Overview

What follows is the latest version of "the Talk." I seem to have been updating variations of this presentation for a very long time. It is an overview of a vision to develop and validate an etiologic classification system for childhood speech sound disorders of currently unknown origin. I first introduce a set of working terms and concepts that constitute the nosological framework for the system. Then, I discuss epidemiologic and other research findings viewed as support for the hypothesis of etiologic subtypes of childhood speech sound disorders.

I hope this review enriches or at least complements each of the thoughtful essays by my colleagues. I thank them in advance for playing nicely with me at points in their discussions where they may need to address the many gaps in theoretical and empirical support for the proposals offered in the following work in progress.

Explanation in Speech Sound Disorders

The American Speech-Language-Hearing Association's recent adoption of the term *speech sound disorders* (SSD) is a welcome solution to the constraints associated with the *articulation disorders versus phonological disorders* dichotomy of the past three decades. The term *SSD* provides a theory-neutral cover term for researchers and clinicians who may, as I do, view SSD as a complex neurodevelopmental disorder. The term *childhood* (or in medical contexts, *pediatric*) *speech sound disorders*, which parallels the term *childhood language disorders*, unifies the study of speech sound disorders of both known (e.g., Down syndrome, cleft palate) and presently unknown origin.

Figure 1–1 is a sketch of four epochs in the history of causality research in childhood speech sound disorders. The first epoch is the 40-year period from the earliest research studies in this country in the 1920s until the many classic studies of the 1950s, in which epidemiologic and descriptive linguistic methods were used to identify and classify children with speech sound errors. Especially toward the end of this period, *distal* causes of speech errors were addressed and research focused primarily on explanatory theories and constructs from articulatory phonetics, speech motor control, and developmental psychology.

In the following perhaps 30-year period, both linguistic descriptions and causal studies of SSD changed markedly. Methods in our discipline included a succession of alternative descriptive, psycholinguistic, and sociolinguistic paradigms from allied disciplines, with markedly decreased interest in the search for distal causes of SSD. Focus clearly shifted to the identification and delineation of core deficits in *proximal* processes that constrain speech acquisition and performance.

A third epoch, lasting perhaps 10 years (note the shrinking shelf-life of epochs), was dubbed the *decade of the brain*. Advances in neuroimaging and other assessment technologies enabled renewed interest in both distal and proximal causal perspectives underlying SSD, especially, in the present context, as it became possible to describe neural correlates of speech sound processing more directly.

Our discipline is currently enjoying the opportunities presented in a fourth epoch—the postgenomic era. Following the successful conclusion of the Human Genome Project in 2001, continuous technical advances make it possible to study the distal origins of many putative sources of SSD. Overviews of the current period often allude to the "Omics," with levels of explanation proceeding downstream from the genome: Genomics > Transcriptomics > Proteomics > Glycomics > Metabalomics > Epigenomics > Phenomics and others. Vernes et al. (2006) report the first example of functional genetic analyses of a gene underlying one subtype of SSD (*FOXP2*), demonstrating the potential of neurodevelopmental research using systems biology.

We take the perspective that an etiologic classification system for SSD is needed if this highly prevalent disorder (to be discussed) is to participate in the scientific and clinical advances being achieved in other

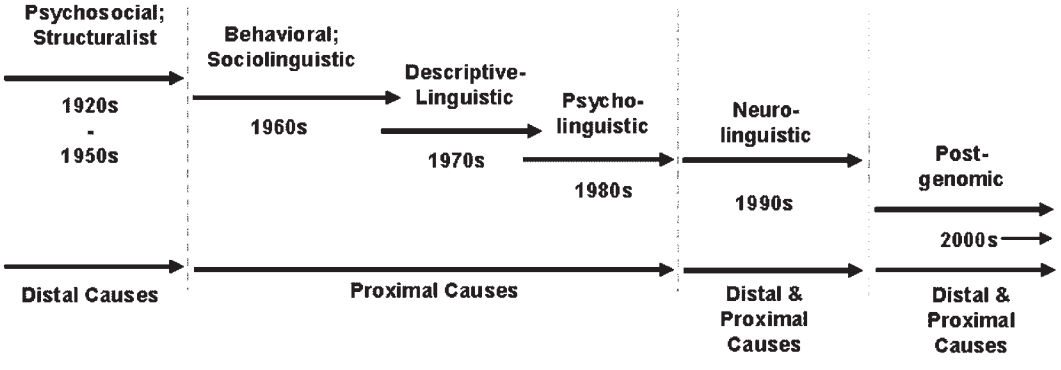


Figure 1–1. Four epochs of causality research in speech sound disorders.

childhood diseases and disorders. The following section describes a research framework proposed for this challenge.

The Speech Disorders Classification System (SDCS)

Speech Disorders Classification System–Typology (SDCS-T)

Figure 1–2 is the Speech Disorders Classification System (SDCS), a framework for research in SSD that has evolved from rudimentary descriptions (Shriberg, 1980, 1982a, 1982b; Shriberg & Kwiatkowski, 1982), a call for speech-genetics research (Shriberg, 1993), and several preliminary presentations (Shriberg, 1994, 1997; Shriberg, Austin, Lewis, McSweeny, & Wilson, 1997b). The left arm of the SDCS, titled SDCS-T, provides a typologic nosology that divides SSD of unknown origin into two subtypes. The more clinically significant subtype is termed *speech delay* (SD) with *delay* highlighting the finding that most children with this subtype of SSD normalize with treatment. The SDCS defines SD as a pattern of speech sound deletions and/or substitutions characteristic of Ingram's (1989) Phonological Stage III that persists past 4 years of age (cf. Shriberg & Kwiatkowski, 1982; Shriberg, Kwiatkowski, & Gruber, 1994). Notice that we use the term SD as one of two subtypes of SSD, whereas SSD and SD typically are used synonymously in the literature. As reviewed shortly, there are few data on the risk and protective factors that predict normalization versus persistence of SD at 6 years of age (Peterson, Pennington, Shriberg, & Boada, in press). Crucially, although speech sound production errors may normalize with treatment, SD places a child at increased risk for literacy delays (Hesketh, 2004; Leitão & Fletcher, 2004; Raitano, Pennington, Tunick, Boada, & Shriberg, 2004; Shriberg & Kwiatkowski, 1988), lowered self-concept (Barrett & Hoops, 1974), and restricted vocational choices (Felsenfeld, Broen, & McGue, 1994).

The second subtype of SSD of currently unknown origin shown in Figure 1–2 is termed *speech errors* (SE). Children with SE have histories of speech sound distortion errors (for English-speaking children typically on sibilants and rhotics) that are not associated with the risk domains documented for SD and that do not interfere with intelligibility. The prevalence of SE below age 9 is estimated at approximately 5% (Shriberg & Austin, 1998). Reviews of the limited epidemiologic data indicate that after 9 years of age, 1 to 2% of adolescents and adults have one or more of a small set of residual distortion errors from prior SD or SE, errors that may persist for a lifetime (Lewis & Shriberg, 1994).

Speech Disorders Classification System–Etiology (SDCS-E)

The right arm of Figure 1–2 is termed the Speech Disorders Classification System–Etiology (SDCS-E). The SDCS-E provides the conceptual framework and working terms for seven etiologic subtypes of SSD. Table 1–1 includes additional speculation on genetic versus environmental contributions underlying each of seven subtypes. The central claim is that SD and SE do not arise from the same monolithic causal domain and that each includes etiologic subtypes. The hypothesis for SD is that it includes five individual and overlapping etiologies, each with one or more distal and proximal origins with risk and protective factors in both genetic and environmental domains.

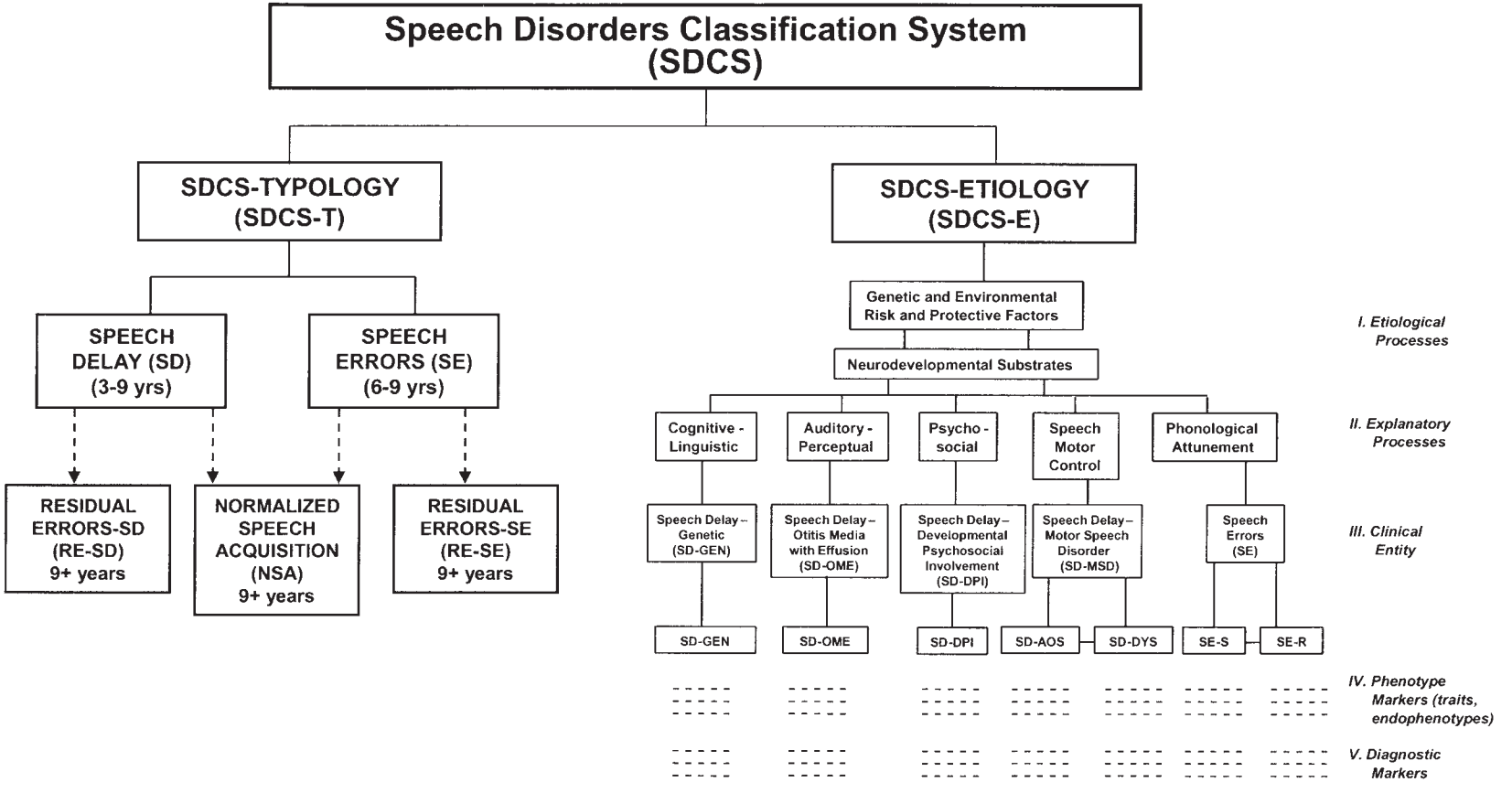


Figure 1–2. A framework for causality research in childhood speech sound disorders.

Table 1–1. Seven Subtypes of Speech Sound Disorders in the Speech Disorders Classification System-Etiology (SDCS-E)

	Working Term	*Abbreviation*	*Primary Origin*	*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–Developmental Psychological Involvement	SD-DPI	Polygenic/ Environmental	Affective-Temperamental
4	Speech Delay–Apraxia of Speech	SD-AOS	Monogenic? Oligogenic?	Speech Motor Control
5	Speech Delay–Dysarthria	SD-DYS	Monogenic? Oligogenic?	Speech Motor Control
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 Speech Sound Disorders	USSD	Any 1–7	Any 1–7

The hypothesis for SE is that it includes two subtypes, each based on a different group of environmental risk factors (Shriberg, 1994).

A set of working terms (and their abbreviations) is used to reference children whose speech delay may be due to one or more of the five proposed distal-proximal origins shown in Figure 1–2 and Table 1–1. The five etiologic subtypes of SD are those associated with (a) cognitive-linguistic processing constraints that may be, in part, *gen*etically transmitted (*SD-GEN*); (b) auditory-perceptual processing constraints that are the consequence of the fluctuant conductive hearing loss associated with early recurrent *o*titis *m*edia with *e*ffusion (*SD-OME*); (c) affective, temperamental processing constraints associated with *d*evelopmental *p*sychosocial *i*nvolvement (*SD-DPI*); (d) speech motor planning/programming constraints consistent with *a*praxia *o*f *s*peech (*SD-AOS*); and (e) speech motor execution constraints consistent with several forms of *dys*arthria (*SD-DYS*). The term *motor speech disorder* (MSD) is used for children suspected to have either or both of the latter two sensorimotor speech disorders. It is important to underscore the epidemiologic observation that a significant proportion of children with SD have involvement in two or more of the five distal and proximal domains.

The two subtypes of *speech errors* (SE) included in the SDCS-E provide classifications for English speakers who have transient or persistent distortions of sibilants (SE-S) and/or rhotics (SE-R). Changing views of handicap and competing service delivery needs have greatly affected research and applied interests in children and adults with SE. Although SE was well studied in the first two epochs delineated in Figure 1–1, persistent speech sound distortions such as dentalized /s/, lateralized /s/, derhotacized /r/, or velarized /l/ are currently viewed as having negligible or minor social consequences. The causal origins of such allophones and their natural histories, however, remain of considerable theoretical interest. We have proposed a variant of attunement theory (phonological attunement) to account for sociodemographic differences observed between children with SD and SE and between children with each of the two proposed subtypes of SE (Shriberg, 1975, 1994).

The dashes in the lower rows of the right arm in Figure 1–2 are placeholders for the research and applied goals of the SDCS-E. Our aims have been to provide diagnostic markers that discriminate each of the five etiologic subtypes of SD, and to develop binary and quantitative phenotypes and endophenotypes for use in molecular genetic studies. As discussed presently, encouraging progress has been made toward filling in the blanks.

Finally, the two cover terms at the bottom of Table 1–1 are needed to differentiate among research samples. Undifferentiated speech sound disorders (USSD) is a useful class term for speakers who may have either SD or SE. Undifferentiated speech delay (USD) is a useful class term for speakers who have or have had SD, but have not been differentiated on the basis of the proposed etiologic subtypes (e.g., SD-GEN, SD-OME, SD-DPI, SD-AOS, SD-DYS).

Epidemiology of Speech Sound Disorders

Prevalence and Persistence of Speech Delay

Figure 1–3 includes prevalence estimates for USD (i.e., speakers who meet criteria for SD, but are undifferentiated relative to subtypes of SD). Methodological details for

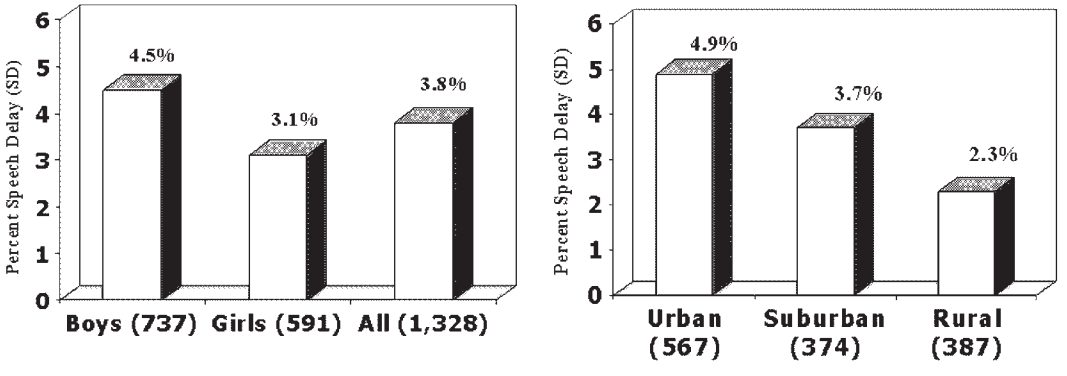


Figure 1–3. Prevalence estimates for Undifferentiated Speech Delay (USD) at six years of age (adapted from Shriberg, Tomblin, & McSweeny, 1999).

the population-based sample from which estimates were obtained are provided in Shriberg, Tomblin, and McSweeny (1999). The prevalence estimate of 3.8% at 6 years of age in the left panel indicates that SD is highly prevalent, with implications for both genetic and environmental explanatory accounts and service delivery needs. Because several of our prospective studies have indicated that approximately 75% of children have normalized their SD by 6 years of age, we estimate that SD occurs in 15 to 16% of children at 3 years of age. A study by Campbell et al. (2003) using the SDCS-T to classify speech disorders cross-validated that projection, reporting a prevalence of SD at age 3 of 15.2%. This latter prevalence estimate is the area approximately equivalent to one-standard deviation below the normal curve, suggesting that speech acquisition is a normally distributed trait with SD reflecting scores below the 16th percentile. From a genetic perspective, as posited in Table 1–1, the mode of genetic transmission for a normally distributed trait is consistent with polygenic, rather than monogenic or oligogenic transmission, in addition to risk associated with environmental sources. The prevalence estimate for males (4.5%) compared to females (3.1%), a ratio of 1.5:1, and the differing prevalence estimates associated with the three geographic strata shown in the right panel in Figure 1–3, further support the need for explanatory models that include both genetic and environmental risk and protective factors. Notice that the prevalence estimate for children from urban strata (4.9%) is more than twice that for children from rural strata (2.3%). Campbell et al. (2003) reported three genetic-environmental risk factors that best predicted SD: male, lower educational level of the mother, and a history of SD in other family members.

The three panels in Figure 1–4 provide preliminary estimates of short- and long-term normalization of SD, with implications for etiologic subtypes of SD (Lewis & Shriberg, 1994). From 9 to 12 years of age, the period when even severe SD should normalize, about 30% of children shown in the two independent subsamples retained distortions of sibilants and rhotics. That figure dropped to approximately 9% from 12 to 18 years. Rhotic errors persisted after 18 years in 9% of children with prior SD, possibly persisting throughout these individuals' lifetimes.

The normalization/persistence data in Figure 1–4 raise questions of considerable interest for explanatory accounts of SSD. Clinical experience indicates that dentalized and lateralized sibilant errors persist in adults. Yet the preliminary estimates in Figure 1–4, which are based on children who had SD, not SE, indicate persistence primarily of rhotic distortions. If reliable, what explanatory mechanisms might account for this difference in the persistence of subclasses of residual errors? Epidemiologic data using population sampling designs could provide such information, particularly as there are now cohorts of adults with untreated SE due to school districts' contemporary definitions of handicap. Later discussion of research findings in SD-GEN will consider related issues.

Emerging Epidemiologic Data for Subtypes of Speech Sound Disorders

We have been continuously updating epidemiologic and speech findings for the hypothesis of etiologic subtypes of SSD. The entries in Table 1–2 are current estimates for five such variables, based on published and unpublished clinical samples from collaborative studies. The question marks indicate cells for which there presently are no available preliminary estimates, mainly due to the lack of emerging diagnostic markers for some SDCS-E subgroups.

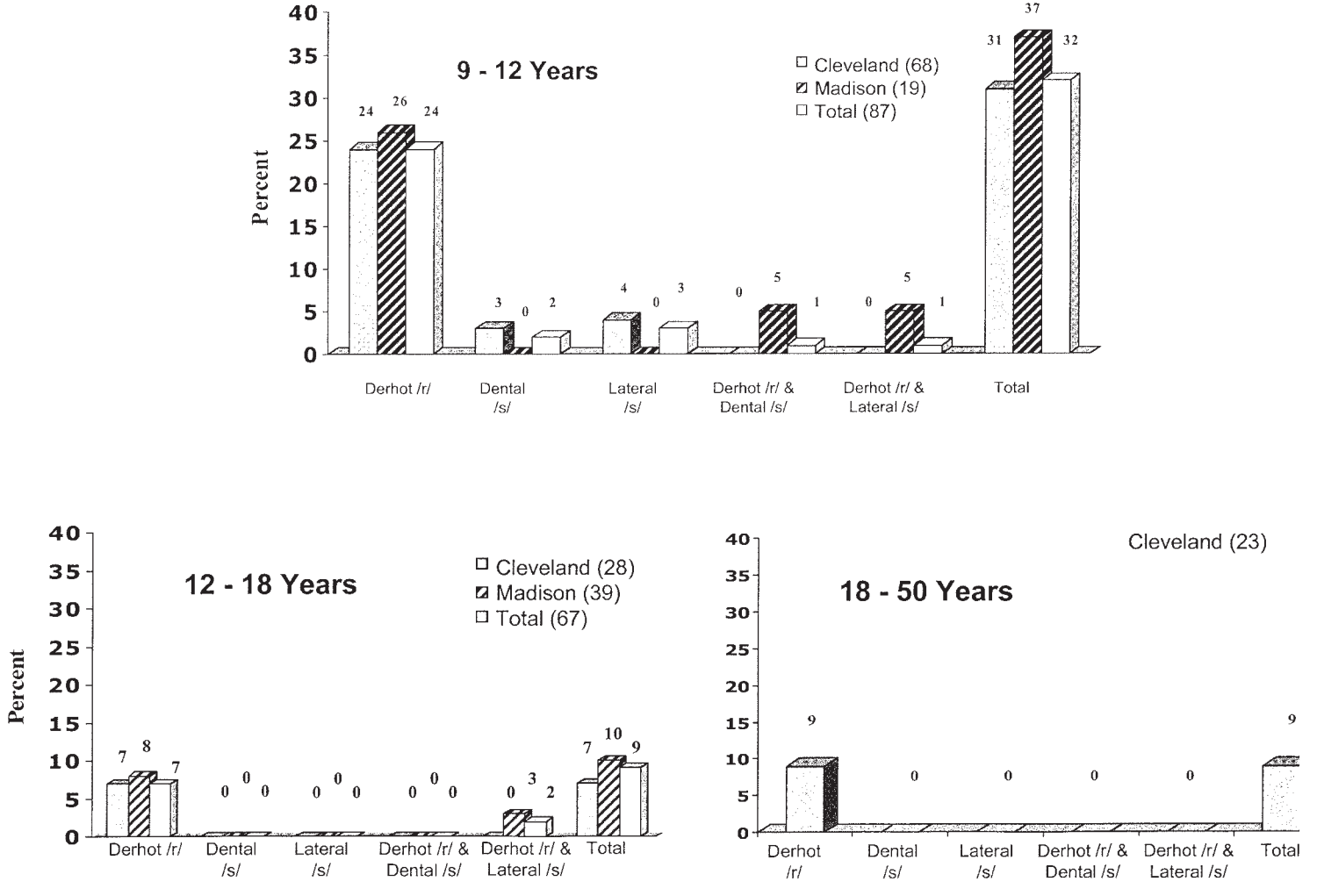


Figure 1–4. Point prevalence estimates for residual speech errors in children with prior SD (RE-SD).

Table 1–2. Epidemiologic Estimates for Seven Proposed Etiological Subtypes of SSD

	Speech Delay (SD)					*Speech Errors (SE)*	
Variables	***SD-GEN***	***SD-OME***	***SD-DPI***	***SD-AOS***	***SD-DYS***	***SE-S***	***SE-R***
Clinical Prevalence	56%	30%	12%	<1%	?	?	?
Sex	M > F	M = F	M > F	M > > F	?	M < F	M > F
Delayed Onset of Speech	NO	NO	NO	YES	?	NO	NO
Language Disorder	YES	YES	YES	YES	?	NO	NO
Normalization of Speech	EARLY	?	LATE	LATE	?	Variable	Variable

Clinical Prevalence

The clinical prevalence estimates in Table 1–2 are the percentages of children with speech delay in study samples who met diagnostic criteria for the five proposed etiologic subtypes. These estimates are based on referrals to one university-affiliated speech clinic (Hauner, Shriberg, Kwiatkowski, & Allen, 2005; Shriberg & Kwiatkowski, 1994). Using SDCS inclusionary markers for each proposed subtype (see later discussion), estimates indicate that SD-GEN (56%), SD-OME (30%), and SD-DPI (12%) account for 98% of children referred for assessment/treatment of SD, with the remaining 2% possibly having apraxia of speech and/or dysarthria. Again, these estimates are based on referral rather than population samples, and are not adjusted for overlapping categories. If cross-validated in other clinics, and perhaps in a large epidemiologic study of speech sound disorders, they are presumably informative for research, clinical training, and treatment. Notably, they suggest that the majority of children with SD would best profit from treatment procedures that address delays in cognitive-linguistic processes (i.e., the proximal causes of SD for SD-GEN; see Figure 1–2 and Table 1–1). They also suggest that a significant percentage of children might require treatment procedures that address alternative or additional speech processing needs.

Sex Ratios

The 1.5:1 boys-to-girls prevalence estimate noted previously for USD (see Figure 1–3) may not obtain for each of the proposed subtypes of SD. It holds for the estimated 68% of children with SD posited to have SD-GEN (56%) or SD-DPI (12%), but not for SD-OME, in which the sex ratio is estimated at 1:1. Boys-to-girls ratios for SD-AOS have been estimated to even more greatly favor boys (Hall, Jordan, & Robin, 1993), but a recent review of 55 cases reported to have genetically-based (i.e., nonidiopathic) SD-AOS occurring in complex neurodevelopmental disorders indicated approximately equal percentages of boys and girls (Shriberg, in press). Finally, as indicated in Table 1–2,

preliminary findings of more boys with SE-R (rhotics) errors and more girls with SE-S (sibilant) errors are viewed as support for an attunement theory of SE discussed elsewhere (Shriberg, 1975, 1994).

Onset of Speech

As indicated in Table 1–2, a significant delay in the onset of speech may be one feature that differentiates SD-AOS from the other proposed subtypes. However severe or unintelligible their speech, children in each of the four other proposed subtypes of SD begin speaking at the expected time. The assumption is that for children who are true positives for SD-AOS, the praxis deficit makes speaking inordinately difficult.

Comorbidity of Language Disorder

Entries in the fourth row of Table 1–2 indicate that children in at least four of the five subgroups of SD are at increased risk for language disorder. As with most other domains shown in Table 1–2, there are few data on language impairment in children posited to have a clinical or subclinical type of dysarthria (SD-DYS). Language impairment is a primary feature differentiating children with SD from those with SE. Of considerable interest in recent genetic research is why some children with SD are spared language impairment, and more generally, what are the important genotype-phenotype relationships across verbal disorders (McGrath et al., 2008; McGrath et al., 2007; Miscimarra et al., 2007; Peterson et al., in press).

Normalization/Persistence

Entries in the fifth row of Table 1–2 are estimates of normalization versus persistence of SD, with implications for explanatory theories and clinical decision making. Presently there are no data on the recovery rates for children differentiated into the five proposed SDCS classifications; retrospective and prospective studies are in process. With the 75% short-term normalization rates for USD referenced previously, and SD-GEN estimated to comprise 56% of clinical referrals, a large percentage of children who normalize may have this subtype of SD. In contrast, the increased severity of involvement in children meeting criteria for SD-DPI (discussed later), and the persistent segmental and especially suprasegmental deficits reported for children with SD-AOS, warrant classifying children in these groups as having late normalization or persistent disorder. Again, data on the natural histories of SE would inform theories of both SE and SD.

Emerging Research Using the SDCS Framework: Overview

To this point, we have proposed that an etiologic classification system for SSD is needed for this highly prevalent disorder to participate in the translational scientific advances emerging for other childhood disorders. What types of evidence in addition to epidemiologic information have been reported supporting the hypothesis of etiologic subtypes of speech sound disorders? The following sections provide brief research overviews and highlight selected methodological and substantive findings. Due to space limitations, the focus is on two of the seven proposed subtypes—SD-GEN and SD-OME—with only brief comment on SD-DPI and SD-AOS. As indicated, there is sparse literature on SD-DYS, and we comment on SE only in the context of the following discussion of SD-GEN.

Emerging Research Using the SDCS Framework: Speech Delay–Genetic (SD-GEN)

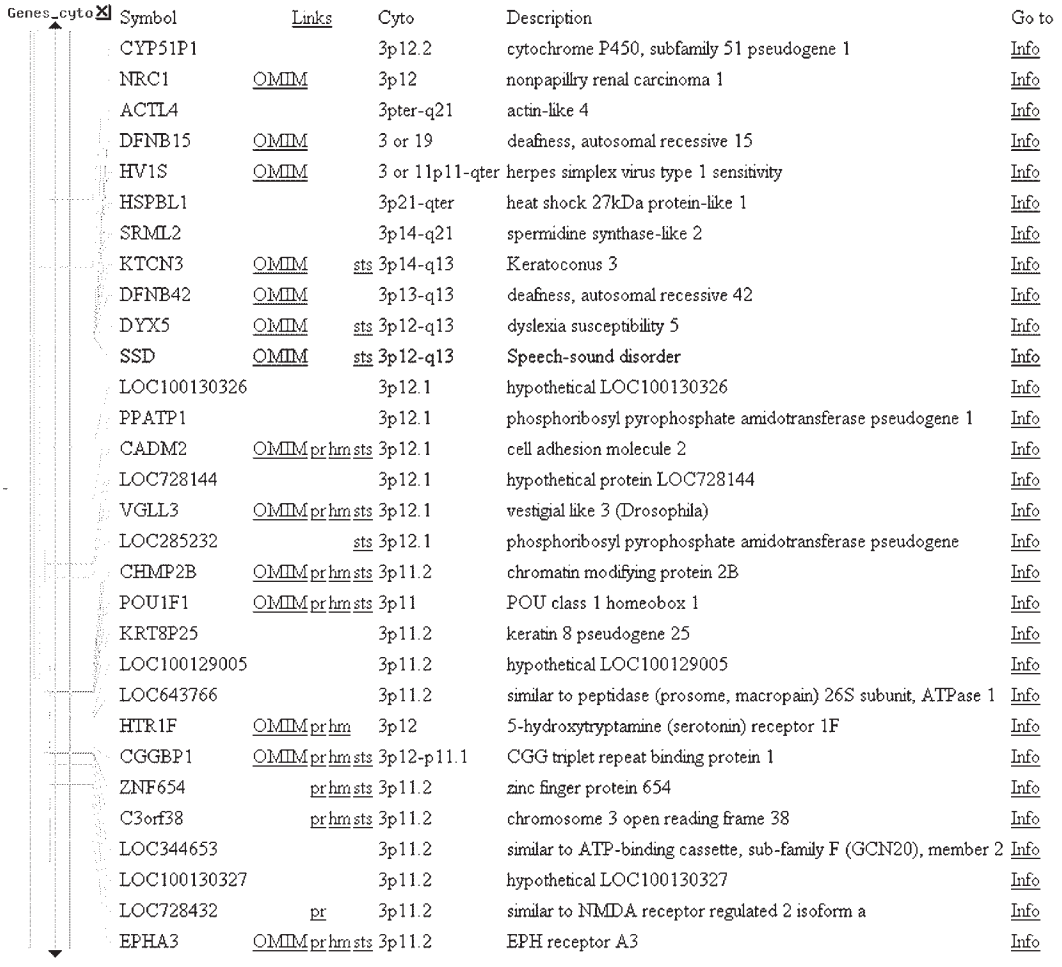
Literature Review

Significant recent progress has been made in the molecular genetics of SD. Behavioral genetic research in the previous decade provided strong support for the likelihood of a genetic form of SD based on findings from familial aggregation studies and twin studies (Stromswold, 1998, 2001). Compelling findings from a twin-adoption study (Felsenfeld & Plomin, 1997) provided strong support for genetic, rather than shared or nonshared environmental, sources of risk for SD in families with histories of verbal trait disorders.

The primary molecular genetic research findings to 2008, using a variety of positional cloning and other methods, have been the identification of significant regions of interest for what we term SD-GEN on four chromosomes. Each of these regions also is reported to be a susceptibility locus for language and/or reading disorders. In Lewis et al. (2006), we provide a glossary of common terms in genetics research and a review of findings, focusing on the limited research in speech-genetics compared to the more extensive genetics literature in other verbal trait disorders. A summary table lists findings from 34 linkage studies of language, reading, and spelling impairment that report susceptibility loci on 11 of the 22 autosomes (1–3, 6, 7, 13, 15, 16, 18, 19, 21). In contrast, our review of linkage findings for SD in Lewis et al. includes only four studies reporting significant or suggestive linkage of SD to regions on chromosomes 1 (1p36: Smith, Pennington, Boada, & Shriberg, 2005), 3 (3p12-q13: Stein et al., 2004), 6 (6p22: Smith et al., 2005), and 15 (15q21: Smith et al., 2005; 15q14: Stein et al., 2006). Candidate genes for SD-GEN, based on their association with reading, language, or speech disorders for these proposed studies include loci on chromosomes 3 (*ROBO1*), 6 (*DCDC2*, *KIAA0319*, *THEM2*), and 15 (*DYX1C1*). As discussed later, separate literatures continue to address the origins of vocal communication catalyzed by the finding that disruptions in the *FOXP2* gene are associated with reported apraxia of speech. Chapter 3 by Barbara Lewis may also be of interest here.

The Mendelian Inheritance in Man database has created a new entry, *Speech Sound Disorder* (*SSD*: MIM %608445), to archive genetic findings for SSD. Figure 1–5 is a sample of the rich information available in MIM, one of many databases and bioinformatic resources used in genetic research. Interested readers are invited to visit the online version of this database (OMIM: www.ncbi.nlm.nih.gov/omim/) and search on "SSD" for more information on this entry. In this view of a susceptibility region of interest for Speech Sound Disorders on chromosome 3 (11 rows from top), there are two nearby regions of interest and genes associated with other verbal trait disorders: the *DYX5* gene above, and (not shown in this display), the *ROBO1* gene, both of which have been linked to dyslexia.

As indicated previously, a number of recent analyses have explored genotype-phenotype associations within and across verbal domains (McGrath et al., 2007; Miscimarra et al., 2007; Peterson et al., in press). For example, using linkage analyses procedures, Miscimarra et al. (2007) demonstrated that the *DYX8* region (1p34-p36) may include genes with pleiotropic (multiple) effects, including SD, language impairment, and reading disorders. Such findings supporting common genetic influences across verbal domains are consistent with the polygenic-environmental causal model posited for SD-GEN in Table 1–1 and the



Genes_cyto	Symbol	Links	Cyto	Description	Go to
	CYP51P1		3p12.2	cytochrome P450, subfamily 51 pseudogene 1	Info
	NRC1	OMIM	3p12	nonpapillry renal carcinoma 1	Info
	ACTL4		3pter-q21	actin-like 4	Info
	DFNB15	OMIM	3 or 19	deafness, autosomal recessive 15	Info
	HV1S	OMIM	3 or 11p11-qter	herpes simplex virus type 1 sensitivity	Info
	HSPBL1		3p21-qter	heat shock 27kDa protein-like 1	Info
	SRML2		3p14-q21	spermidine synthase-like 2	Info
	KTCN3	OMIM sts	3p14-q13	Keratoconus 3	Info
	DFNB42	OMIM	3p13-q13	deafness, autosomal recessive 42	Info
	DYX5	OMIM sts	3p12-q13	dyslexia susceptibility 5	Info
	SSD	OMIM sts	3p12-q13	Speech-sound disorder	Info
	LOC100130326		3p12.1	hypothetical LOC100130326	Info
	PPATP1		3p12.1	phosphoribosyl pyrophosphate amidotransferase pseudogene 1	Info
	CADM2	OMIM pr hm sts	3p12.1	cell adhesion molecule 2	Info
	LOC728144		3p12.1	hypothetical protein LOC728144	Info
	VGLL3	OMIM pr hm sts	3p12.1	vestigial like 3 (Drosophila)	Info
	LOC285232	sts	3p12.1	phosphoribosyl pyrophosphate amidotransferase pseudogene	Info
	CHMP2B	OMIM pr hm sts	3p11.2	chromatin modifying protein 2B	Info
	POU1F1	OMIM pr hm sts	3p11	POU class 1 homeobox 1	Info
	KRT8P25		3p11.2	keratin 8 pseudogene 25	Info
	LOC100129005		3p11.2	hypothetical LOC100129005	Info
	LOC643766		3p11.2	similar to peptidase (prosome, macropain) 26S subunit, ATPase 1	Info
	HTR1F	OMIM pr hm	3p12	5-hydroxytryptamine (serotonin) receptor 1F	Info
	CGGBP1	OMIM pr hm sts	3p12-p11.1	CGG triplet repeat binding protein 1	Info
	ZNF654	pr hm sts	3p11.2	zinc finger protein 654	Info
	C3orf38	pr hm sts	3p11.2	chromosome 3 open reading frame 38	Info
	LOC344653		3p11.2	similar to ATP-binding cassette, sub-family F (GCN20), member 2	Info
	LOC100130327		3p11.2	hypothetical LOC100130327	Info
	LOC728432	pr	3p11.2	similar to NMDA receptor regulated 2 isoform a	Info
	EPHA3	OMIM pr hm sts	3p11.2	EPH receptor A3	Info

Figure 1–5. Entry for *Speech Sound Disorders* (%608445) in Mendelian Inheritance in Man (MIM). This figure is included only to illustrate a display from one of the most frequently consulted bioinformatic sources. Definitions for column headings and other terms are available at the online site: www.ncbi.nlm.nih.gov/omim/

contemporary perspective of "generalist genes" (Butcher, Kennedy, & Plomin, 2006).

Phenotypes for SD-GEN

A primary goal of our collaborative genetic research in SD-GEN has been to develop quantitative phenotypes that are sensitive to and specific for this proposed subtype of SD (Shriberg, 1993). The goal in family-based genetic designs is to assess relevant family members of the proband using measures that provide one or more quantitative indices for each sign of the disorder. Obtaining such information from direct behavioral testing of individuals who are at risk for the disorder, are currently expressing the disorder, or who have normalized prior disorder is preferable to using case records data (Barry, Yasin,

& Bishop, 2007; Lewis et al., 2007; Plante Shenkman, & Clark, 1996). Phenotypes must be sensitive to all levels of severity of expression of the disorder, as adjusted for possible age, gender, and other sociodemographic variables, but they may or may not be specific for it (i.e., they may be narrower or more broad relative to the domain of interest).

Several phenotypes have been used for family members of different ages in collaborative speech-genetics studies. For probands and young siblings assessed during the developmental period (years 3–6) in which misarticulation profiles are especially sensitive and specific for SD, two sets of phenotypes have been productive in the molecular genetic studies with colleagues just reviewed: the binary SDCS-T phenotype (Normal Speech Acquisition [NSA] versus Speech Delay [SD]; Shriberg et al., 1997b) and two continuous phenotypes (*ZPCC* and *ZPCCR*; z-scores for Percentage of Consonants Correct [PCC] and Percentage of Consonants Correct-Revised [PCCR]; Shriberg, Austin, Lewis, McSweeny, & Wilson, 1997a). For ages 6 to 9 years, when speech production errors may be nearly normalized with treatment, two continuous phenotypes developed to be maximally sensitive to persistent SD errors have also been productive: *Speech1* and *Speech2*. The latter two phenotypes (log of the odds and probability of having prior SD, respectively) were obtained from a 7-variable composite derived from a multivariate logistic regression using 17 out of 120 speech metrics that had the highest diagnostic accuracy for a sample of 759 speakers with prior SD (Smith et al., 2005).

Endophenotypes for Verbal Trait Disorders

Significant linkage findings in verbal trait disorders have most often been made to several widely used nonword repetition tasks (Newbury, Bishop, & Monaco, 2005). A significant confound with such tasks in speech-genetics research is that nonword repetition errors cannot be disambiguated from misarticulations. We have reported psychometric and substantive findings for an 18-item syllable repetition task that requires respondents to repeat nonwords comprised of only four Early-8 consonants (/b/, /d/, /m/, /n/) and one nonscored vowel (/ɑ/) in two-, three-, and four-syllable words (e.g., /bɑmɑdɑ/; Shriberg et al., 2008). Responses to this task, titled the Syllable Repetition Task (SRT), and to a comparison measure, the Nonword Repetition Task (NRT; Dollaghan & Campbell, 1998), were obtained from 158 children assessed in a collaborative physiology study, including 95 preschool participants with SD. Findings from three substudies support the construct and concurrent validity of the SRT and its internal reliability. All children had the four consonants in their inventories. Effect sizes estimating its ability to discriminate comorbid expressive language disorder from no language disorder were significant and comparable in magnitudes to those obtained with the NRT.

Additional analyses indicated that the SRT can aid in dissecting the speech processing constraints underlying poor performance on nonword repetition tasks. Briefly, we used differences in item length (2-, 3-, 4-syllable nonwords), error type (within versus across class manner substitutions), and articulatory difficulty (i.e., two-syllable items with homorganic [same place] versus homotypic [same manner] consonants) to assess the level of support for errors reflecting processing constraints at three phases prior to articulatory execution: auditory-perceptual encoding, storage-retrieval, and articulatory planning-programming. Findings provided strong support for auditory-

perceptual encoding deficits underlying repetition errors of children with typical and delayed speech, mixed support for memorial processes, and no support for articulatory planning/programming deficits. On memorial processing, although longer SRT words generally were more difficult to imitate correctly, twenty-four percent of the 158 participants (87% of whom had SD) had repetition errors on at least half of the 16 consonant targets in the two-syllable nonwords (e.g., /dɑmɑ/). We interpreted these findings as arguing against a simple memory capacity constraint explanation for poor nonword repetition of these short CVCV words. On auditory-perceptual processing, the substitution errors of children with typical speech-language development more often retained the correct manner feature of the target consonant (e.g., /d/ for /b/, rather than either of the two nasal consonants for /b/) compared to the percentage of within-class substitution errors made by participants with speech-language impairment. We suggest that the SRT may be a useful endophenotypic metric for speech-genetics research, as well as for research with speakers with disorders of any type who have limited phonetic inventories or misarticulations.

Diagnostic Markers for SD-GEN

Recall that as indicated at the bottom of the right arm of the SDCS-E (see Figure 1–2), a primary research need is for diagnostic markers to identify children with one or more of the five proposed subtypes of SD. Diagnostic markers have to be sensitive to SD at all levels of severity of expression. Crucially, unlike phenotype markers, they must be specific for each subtype. We have made some progress identifying diagnostic markers for SD-GEN for use in genetic research.

A Diagnostic Marker for Children with SD-GEN

In Shriberg et al. (2005), we reported diagnostic marker findings for children at risk for SD-GEN. We divided 72 preschool children expressing SD into two groups comparable in age, gender, language status, and speech severity, but differing in family history of speech-language-reading disorder. Group 1 had two or more nuclear family members with histories of or active speech-language-reading disorder, whereas Group 2 had no nuclear family members that met this criterion. Although the two groups were assembled to have similar levels of severity of involvement (Group 1: PCC = 70.0% [10.3]; Group 2: PCC = 71.6% [10.2]), there were statistically significant between-group differences in their absolute and relative percentages of omission errors. Group 1 children, who presumably had higher liabilities for SD-GEN than Group 2 children, had significantly higher percentages of relative omission errors, particularly on the Late-8 (i.e., most difficult) speech sounds. The significant effect size for this latter comparison was 0.86 (C.I. = 0.35–1.37).

In addition to its diagnostic significance, we interpret these findings as support for the core claim (see Figure 1–2 and Table 1–1) that SD-GEN is due to genetically transmitted cognitive-linguistic constraints affecting phonological processing. We propose that speech sound omissions (compared to speech sound substitutions and distortions) reflect significant deficits in encoding and/or storage-retrieval processes. Literature support associating omissions with cognitive constraints includes the widely attested findings of proportionally more speech sound omissions in cognitive disability (e.g., Shriberg & Widder, 1990) and in the higher percentage of omissions in children with comorbid SD and language

impairment. Speech sound omissions were also more prevalent in children with lowered performance on the SRT, the nonsense word task described above, which appears to be sensitive to individual differences in cognitive-linguistic aspects of speech processing. The omission marker has been cross-validated in an unpublished study that included 95 participants with SD divided by familial aggregation status.

Acoustic Markers to Recover the Phenotype in Residual Speech Errors

What speech signs or signatures might be used to recover SD versus SE origins in older speakers who have normalized or nearly normalized sibilant or rhotic distortions? Recall in Table 1–1 that SD-GEN is posited to have genetic origins, whereas the distal and proximal origins of SE are posited to be moderated by environmental risk and protective factors.

Figure 1–6 provides summary data from two study series attempting to determine if there were acoustic signatures of former SD versus former SE in speakers with residual distortion errors on rhotics (i.e., RE-R) or sibilants (i.e., RE-S). We tested several groups of adolescents including speakers whose speech histories were documented from our clinic records or school records as having either prior SD or prior SE and control children from the same classrooms. Both narrow phonetic transcription and acoustic methods were used to classify the speech tokens from word lists of speakers with normal or normalized /ɝ/ and those with prior /s/ errors.

As shown in Figure 1–6, /ɝ/ tokens were quantified acoustically by subtracting F2 from F3 and standardizing the result (z-score) using age × sex reference data (Flipsen, Shriberg, Weismer, Karlsson, & McSweeny, 2001). A zF3–F2 value of 3.0 provided excellent discrimination between tokens transcribed perceptually as correct /ɝ/ productions (<3.0) and derhotacized /ɝ/ productions (>3.0) yielding sensitivity/specificity estimates of 95% and 94%, respectively. Moreover, a zF3–F2 cutpoint of 6.0 provided good discrimination between the perceptually derhotacized /ɝ/ tokens of speakers with RE-SD (<6.0) versus RE-SE (>6.0) speech histories (sensitivity/specificity estimates of 85% and 79%, respectively). Notice that the /ɝ/ tokens from the typical speech control group and the normalized speech group had z-score values below 3.0. Crucially, the /ɝ/ tokens of speakers with RE-SD were mostly below 6.0, whereas the /ɝ/ tokens of speakers with RE-SE were mostly above 6.0. Thus, the persistent /ɝ/ distortions of speakers with prior SE were acoustically most discrepant from typically produced /ɝ/ productions.

As shown in Figure 1–6, trends were in the same direction for /s/ productions of adolescents with former SD versus those with former SE measured acoustically using the first spectral moment (M1; Milenkovic, 1996). All tokens from the adolescent speakers were transcribed as perceptually correct, supporting the previous epidemiologic data indicating fewer residual sibilant than rhotic distortion errors in adolescents. Nevertheless, compared to the perceptually correct /s/ tokens from control speakers, the perceptually correct /s/ tokens from the speakers who had prior SE (see Figure 1–6, lower right panel) had notably higher z Moment 1 values compared to those from the speakers who had prior SD.

These /ɝ/ and /s/ findings suggest the possibility of acoustic signatures that may provide the specificity needed to classify family members correctly for speech-genetics

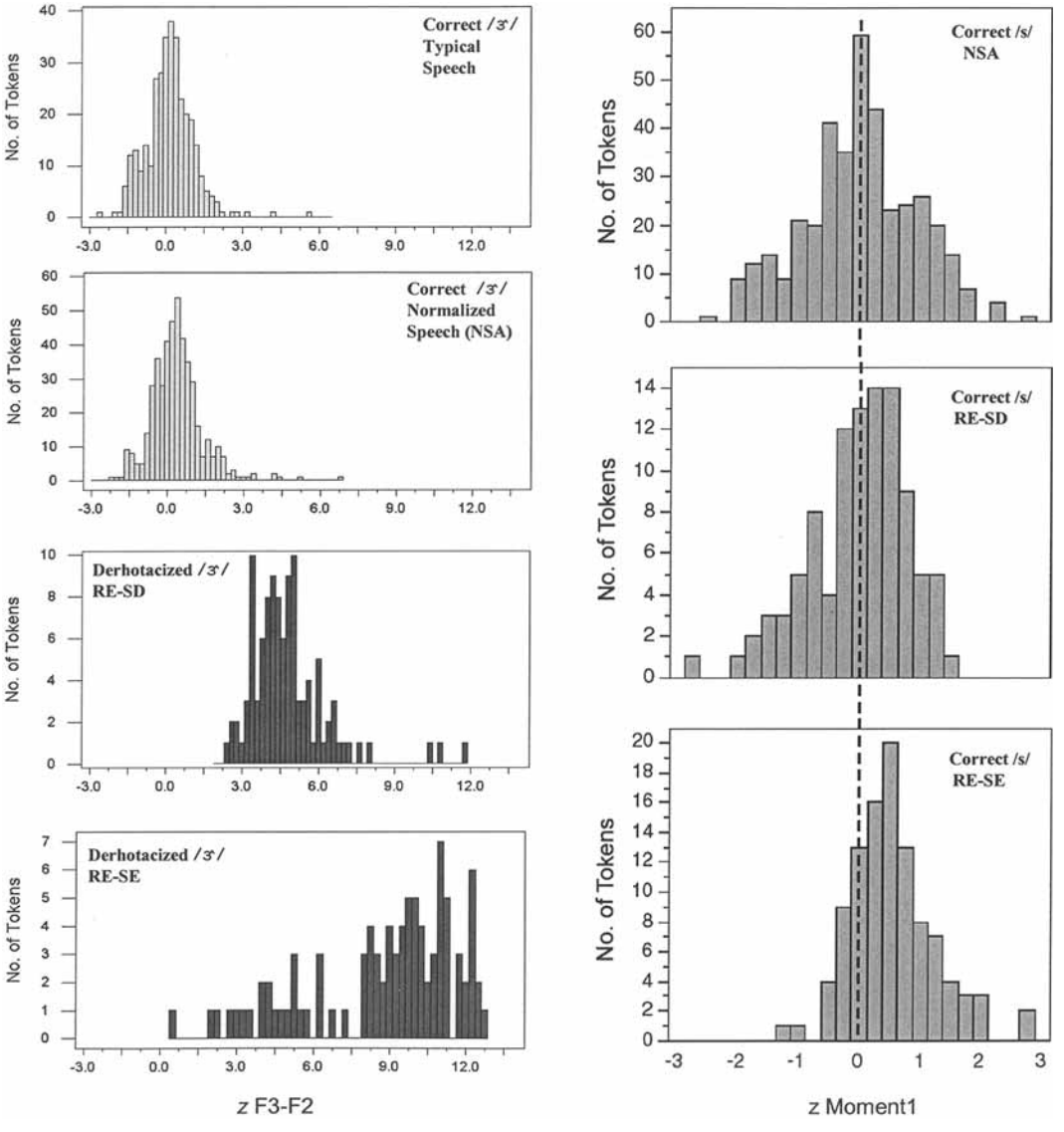


Figure 1–6. Recovery of the speech phenotypes in /ɝ/ and /s/ productions in older speakers. The panels on the left side include the number of tokens at each standardized value (zF3-F2) produced by participants in each of four speaker groups. The panels on the right side include the number of tokens at each standardized value (z Moment 1) produced by participants in each of three speaker groups.

studies. Studies in process are also pursuing implications of the findings in Figure 1–6 in their own right as discussed elsewhere (Karlsson, Shriberg, Flipsen, & McSweeny, 2002; Shriberg, Flipsen, Karlsson, & McSweeny, 2001). There are a number of cognitive and

sensorimotor developmental frameworks that would predict that early distortions are more resistant to change than early errors of omission or substitution. Although considered more detrimental for intelligibility than distortion errors, early omissions of or substitutions for Late-8 sounds—as occurs in SD—may actually have a better prognosis for complete normalization than the early speech sound distortions that occur in SE.

Emerging Research Using the SDCS Framework: Speech Delay–Otitis Media with Effusion (SD-OME)

Literature Review

The hypothesis that early recurrent OME places a child at increased risk for SSD is based primarily on the assumption that the fluctuant conductive hearing loss that may accompany OME can affect the development of veridical and stable phonological representations (Shriberg, 1987). As indicated in Table 1–1, such proximal processes are presumed to have their origins in both polygenetic and environmental risk factors. In a review of 27 OME-speech studies, we concluded that support for *correlative* associations among early OME, hearing loss, and speech delay was equivocal, and that support for *causal* associations remained undocumented (Shriberg, Flipsen, et al., 2000). This is essentially the position of several large-scale prospective studies that have concluded that the mild hearing loss that may occur during episodes of early frequent OME is not a risk factor for early or later impairments in speech, language, academics, or social function. Variants of this conclusion have been expressed in a comprehensive literature review (Roberts, Hunter, et al., 2004), a meta-analysis (Roberts, Rosenfeld, & Zeisel, 2004), an updated set of clinical practice guidelines (Rosenfeld et al., 2004), and, most recently, in a long-term follow-up study of cohorts in the Pittsburgh otitis media project (Paradise et al., 2007).

A consistent trend in smaller scale studies of outcomes for children with significant histories of early frequent OME and hearing loss, however, is for study participants to have significantly lowered performance on cognitive and auditory perception tasks. Three research examples illustrate this trend. Nittrouer and Burton (2005) reported that 5-year-old children with histories of OME and low socioeconomic status scored lower than a control group on tasks involving speech perception, verbal working memory, and sentence comprehension. Gravel et al. (2006) reported that OME and early hearing loss was significantly associated with several measures of auditory processing in children assessed at school age, including measures of extended high-frequency hearing and measures assessing brainstem auditory pathways. Majerus et al. (2005) in a study of 8-year-old children with histories of early recurrent OME reported normal performance on short-term memory and new word learning tasks, but small, statistically significant performance decrements on several phonological processing tasks. These latter authors suggested that one negative outcome of OME appears to be ". . . subtle impairments at the level of perceptual-phonologic analysis . . . " (p. 473).

Is Mild Hearing Loss a Risk Factor for Speech Delay?

How can we reconcile the negative risk findings for mild hearing loss reported in the large-scale, prospective studies of OME with the positive risk findings reported

from small-scale retrospective or ambispective studies using convenience samples? Review of the hearing loss information in our prior and continuing research collaborations prompted us to examine the OME literature for the rationales used to subgroup children by hearing loss histories in both large-group and small-group studies, including the classic paper by Fria, Cantekin, and Eichler (1985) and the detailed information in Gravel and Wallace (2000). We wondered if the independent variable of *mild* conductive hearing loss based on the pure-tone average (PTA) metric may be the source of important methodological differences among OME outcome studies. Some differences we found in the computation of PTA across OME outcome studies include: (a) the number of frequencies tested (3 or 4), (b) the frequencies used to compute the PTA (.5K, 1K, 2K, or 4K), (c) whether the PTA is used as the index if there is greater than a 20 db HL difference in the better ear between any two frequencies, (d) differences in the cutoff levels used to convert PTA values to the ordinal, adjectival classifications for hearing loss (i.e., *mild* versus *moderate* conductive hearing loss), and (e) other testing differences, including the number of hearing evaluations available, the age(s) at which one or more PTAs were obtained, methods used to average multiple PTAs or to select the worst PTA as the primary independent variable.

In recent collaborative research, we explored the implications of prior fluctuant hearing loss on speech outcomes in subsamples of 60 children in each of two prospectively assessed otitis media projects: the Chapel Hill (Roberts, Burchinal, Koch, Footo, & Henderson, 1988) and the Pittsburgh (Paradise et al., 2000) studies. Based on prior collaborative research with the Dallas otitis media study (Shriberg, Friel-Patti, Flipsen, & Brown, 2000) and preliminary analyses of pure tone averages available in the Chapel Hill and Pittsburgh projects, we defined children as having *typical* hearing or (*negligible* hearing loss) if all of their PTAs during the first three years of life ranged from 0 to 24 dB HL. Participants who had at least one PTA from 35 to 45 db HL during this period were classified as having *mild-moderate* hearing loss. Participants in each subsample who did not meet either criteria (i.e., 25-34 db HL and above 45 db HL) were excluded from further analyses.

Figure 1–7A provides speech profiles (PCCR calculated on the Goldman-Fristoe Test of Articulation-2 [GFTA-2]; Goldman & Fristoe, 2000) at 3 years of age for the children from the Chapel Hill study. Group 1 (n = 9; filled circles) participants had typical hearing levels (0-24 dB HL) as assessed from 6 to 36 months and Group 2 (n = 8; open circles) participants had PTAs meeting criteria for mild-moderate hearing loss (35-45 dB HL) on at least one audiologic evaluation. Figure 1–7B provides comparable GFTA-2 data from the Pittsburgh database (Group 1: n = 10; Group 2: n = 6). Over half (57%) of the Group 2 participants in the two datasets had hearing loss from 35 to 40 db HL (i.e., within the standard 40 db HL upper limit for mild hearing loss). Two trends in these independent samples are interpreted as support for the hypothesis that mild-moderate hearing loss associated with OME places a child at increased risk for SD.

First, as shown for both datasets, notably in Figure 1–7A, Group 2 participants had markedly lower average percentages of consonants correct (i.e., ignoring distortions) compared to participants in Group 1. The statistically significant mean between-group differences for each developmental sound class in the top section of Figure 1–7A (percentaged separately for Singletons [S], Clusters [C], and Total [T]) have a "box" drawn

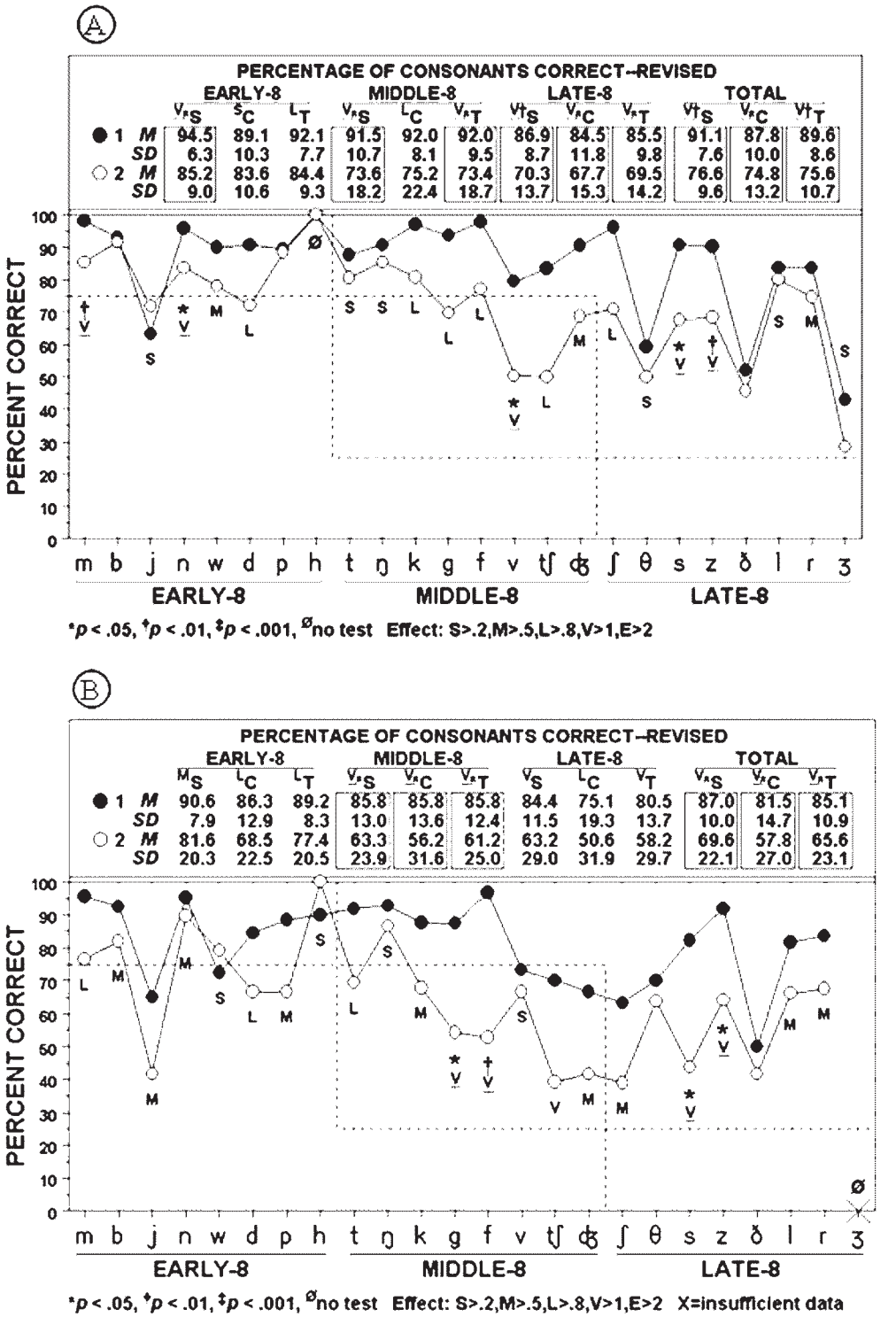


Figure 1–7. Early fluctuant mild-moderate hearing loss as a risk factor for speech delay at three years of age. The data in (**A**) are from the Chapel Hill database (Roberts, Burchinal, Koch, Footo, & Henderson, 1988); the data in (**B**) are from the Pittsburgh database (Paradise et al., 2000).

around them. Conventional inferential statistical symbols and underscored capital letters (*S*: Small; *M*: Moderate; *L*: Large; *V*: Very Large; and *E*: Extremely Large) indicate the magnitudes of significant t-tests and effect sizes, respectively. The significant effect size for the total PCCR was 1.21, especially large for small sample comparisons. Trends for the Pittsburgh data (see Figure 1–7B) were similar, including a significant effect size of 1.29 for total PCCR. Notice that the means for both groups in the two studies are comparable, with most Group 1 children scoring above 85% (typical for 3-year-old children on this speech measure), whereas Group 2 children scored approximately 15–20% lower, in the range reported for children with SD (Shriberg et al., 1997a).

Significant between-group differences in the percentages of correct /s/ and /z/ productions were also evident in both datasets in Figure 1–7. Group 2 participants averaged approximately 20% lower in the atypical 45% to 70% correct range. The magnitudes of the significant effect sizes for the four sibilant comparisons ranged from 1.11 to 1.57. We have reported perceptual (Shriberg & Smith, 1983; Thielke & Shriberg, 1990) and acoustic (Shriberg et al., 2003) data indicating that differences in sibilant production may be one of several possible diagnostic markers of SD-OME. Although considered preliminary due to cell sizes, these are our first data linking mild-moderate hearing loss to later deficits in sibilant production. We interpret findings as reflecting Group 2 participants' reduced attention to the salience of fricative energy in the 4kHz region and above. Again, although the large-scale studies have concluded that mild hearing loss is not a risk factor for SD, over half of the Group 2 children (8/14 = 57%) in these small subsamples had fluctuant hearing loss of 35 to 40 dB HL and all had fluctuant losses below 45 db HL.

Summary and Research Directions

Our current research perspective on the important public health issue in early recurrent OME (i.e., "watchful waiting" versus insertion of tympanostomy tubes) focuses on the need to determine the level and profile of hearing loss that places a child at risk for SD. Auditory perceptual constraints on phonological representations are clearly the relevant primitives in the causal pathways from hearing loss to speech production errors (Clarkson, Eimas, & Marean, 1989), and more generally, in current models of the development (Guenther, 2006) and persistence (Kenney, Barac-Cikoja, Finnegan, Jeffries, & Ludlow, 2006) of speech disorder. If replicated in larger study samples, the findings reviewed may explain why it has been so difficult to document the validity of this proposed subtype of SD. In an invited commentary on the influential Paradise and colleagues 2007 paper, Berman (2007) noted: "Since a hearing loss of 40 dB or higher was uncommon among patients in the study by Paradise and colleagues, it could not address the question of whether this level of hearing loss also leads to impairments" (p. 301). If replicated in prospective studies, the preliminary findings in Figure 1–7 would suggest that an early mild-moderate hearing loss of 35 to 45 dB HL is a risk factor for SD.

Emerging Research Using the SDCS Framework: Speech Delay–Developmental Psychosocial Involvement (SD-DPI)

Literature Review

As indicated previously, due to space constraints we have elected to focus on SD-GEN

and SD-OME, with only brief comments on SD-DPI and SD-AOS. The hypothesis of a subtype of SSD in which psychosocial processes are the primary domain in explanatory accounts and central for treatment planning has been difficult to test. As indicated in Table 1–1, such proximal processes are presumed to have their origins in both polygenetic and environmental risk factors. The working term for this proposed etiologic subtype, Speech Delay–Developmental Psychosocial Involvement (SD-DPI), was coined expressly to avoid the concept of psychopathology or emotional disorder. Rather, we have borrowed from the personality and temperament literatures, which include dimensions such as *mood*, *negative emotionality*, *approach-withdrawal*, *distractibility*, *attention span*, *task persistence*, and *adaptability*. It has seemed that such constructs have been useful to describe independent variables that are risk factors for successful treatment outcomes in our clinical studies of speech delay (Kwiatkowski & Shriberg, 1993, 1998). Contemporary studies have assessed individual differences in temperament as a risk factor or correlate of delayed language development (e.g., Caulfield, Fischel, DeBaryshe, & Whithurst, 1989; Paul & Kellogg, 1997) and stuttering (Anderson, Pellowski, Conture, & Kelly, 2003; Embrechts, Ebben, Franke, & van de Poel, 2000; Lewis & Goldberg, 1997), but as suggested in Figure 1–1, there have been few studies in recent decades on personality or temperament differences and speech sound disorder.

Diagnostic Markers for SD-DPI

Using parental report and clinical records, we found that 29 of 245 children (12%) seen for speech evaluation and treatment in our university speech clinic during an 18-year period met a set of temperament-based criteria for SD-DPI (Hauner et al., 2005). This percentage of children was larger than we expected; these data are the source of the clinical prevalence entry for SD-DPI in Table 1–2. The SD-DPI groups included children who met criteria for either *approach-related negative affect* or *withdrawal-related negative affect* (Goldsmith, Lemery, & Essex, 2004). We assembled a comparison group of 87 children with speech delay from this database, matched to the SD-DPI group in age, gender, and SDCS classification (i.e., SD or an intermediate classification termed NSA/SD).

Speech analyses using a suite of descriptive measures indicated that children meeting criteria for SD-DPI had significantly more severe speech involvement compared to controls with SD. Their modal profile was an across the board delay of about an additional one year, compared to the control group of children with USD not including SD-DPI. They scored lower than the comparison group in each of the three developmental speech classes (Early-8, Middle-8, Late-8) and had significantly lower total PCC scores ($p < .01$; effect size = .57). Until we computed the clinical prevalence estimate for SD-DPI of 12%, we had assumed that such children would comprise a much smaller percentage of children with SD, and that they would likely have less severe speech delay, at least as compared to children suspected to have SD-GEN and SD-OME.

Although we have not, to date, identified a unique speech or prosody-voice marker for SD-DPI, the unexpected severity feature of SD-DPI is of significant interest for theory and practice. Clearly, more research is needed to cross-validate these initial findings and to design controlled studies of psychosocial processes as possible risk and protective variables in speech delay.

Emerging Research Using the SDCS Framework: Speech Delay–Apraxia of Speech (SD-AOS)

Literature Review

Research and particularly clinical concern for apraxia of speech in children has increased significantly in the past two decades (Shriberg & Campbell, 2003). Whereas *Developmental Verbal Dyspraxia* (*DVD*) remains the classification term in medical contexts and most other countries, a position statement by the American Speech-Language-Hearing Association (2007) endorsed the term *Childhood Apraxia of Speech* (*CAS*). The working term SD-AOS references the same group of children as CAS and these terms will be used synonymously in the following comments.

The primary constraint in CAS research and applied clinical decision making is the lack of a set of inclusionary/exclusionary criteria to classify speakers as positive for this disorder (American Speech-Language-Hearing Association, 2007). From a research perspective, differentiating SD-AOS from dysarthria (SD-DYS) is a major research need discussed elsewhere (Shriberg, in press). Our perspective on this issue is that the problem is due to the focus on CAS as an idiopathic speech disorder, neglecting the potential informativeness of research in CAS as a secondary disorder in complex neurodevelopmental contexts.

Our proposed solution to the circularity (Guyette & Diedrich, 1981) or tautology (McNeil, Robin, & Schmidt, 1997) problem in CAS research and the escalating high rates of false positives in contemporary clinical practice (Shriberg & McSweeny, 2002), is the four-phase research design illustrated in Figure 1–8. In the first ("1") phase, we have begun to describe the core features of apraxia of speech as it occurs in adult AOS, in CAS following pediatric neurologic disorders, and in CAS in complex neurodevelopmental contexts (Potter, Lazarus, Johnson, Steiner, & Shriberg, 2008; Shriberg et al., 2006; Shriberg, Jakielski, & El-Shanti, 2008; Shriberg, Jakielski, & Tilkens, 2009; Shriberg & Potter, 2008). For a related discussion, also see Chapter 7 by Velleman and colleagues in this volume. The assumption is that a disorder of speech praxis should have features that are common to both acquired and developmental subtypes, with developmental issues likely moderating severity of expression of the core features. Critical to this approach is use of a well-developed speech assessment protocol that includes the same perceptual and acoustic measures to assess all forms of CAS across the lifespan. We have developed perceptual- and acoustic-based analytics to test alternative perspectives on the precision and stability of spatiotemporal signs in the speech and prosody-voice profiles of speakers suspected to have apraxia of speech. Findings from the first phase are used in the second phase (see Figure 1–8) to identify and develop the criteria that qualify participants as having idiopathic CAS. Findings from these four forms of CAS are expected to inform third phase studies of the genetic and neural substrates underlying the pathobiology of apraxia of speech (for overviews of *FOXP2* research, see Fisher, 2005, 2006; Fisher, Lai, & Monaco, 2003; for an example of systems biology to early 2008 see Groszer et al., 2008). The fourth phase focuses on applied methods for assessment, treatment, and prevention. Shriberg (in press) includes rationale for the framework and a review of 55 cases of CAS occurring in genetic-based neurodevelopmental contexts.

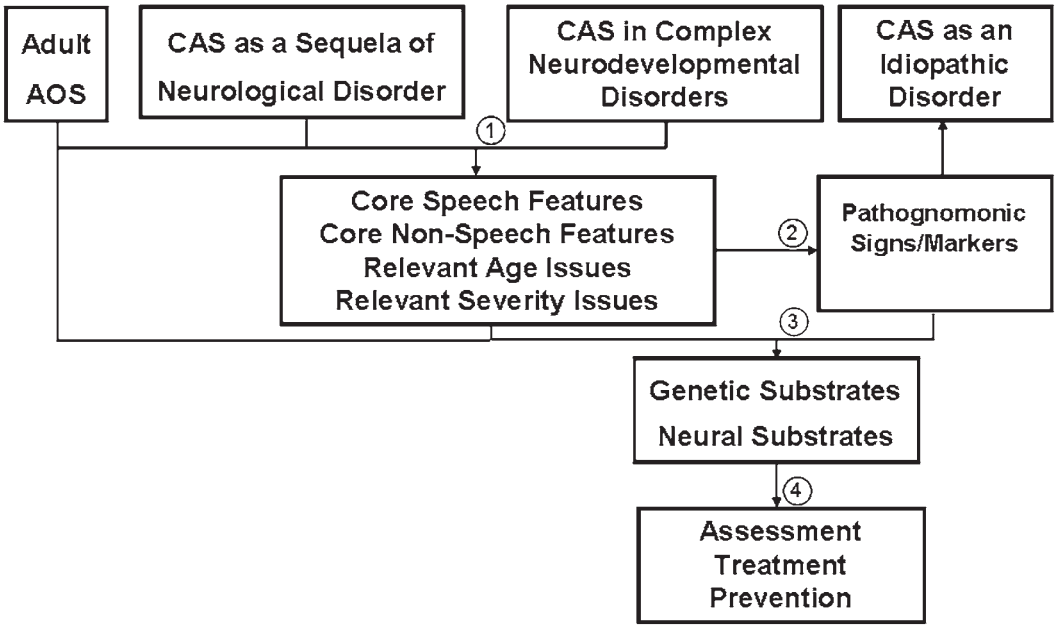


Figure 1–8. A neurodevelopmental framework for research in childhood apraxia of speech. Reprinted with permission from Shriberg, L. D. (in press), A Neurodevelopmental Framework for Research in Childhood Apraxia of Speech. In B. Maassen and P. van Lieshout (Eds.), *Speech Motor Control: New Development in Basic and Applied Research*. Oxford University Press.

Some Translational Needs in SSD

This progress report has described a diagnostic classification system for childhood speech sound disorders and a sample of findings gathered within this framework. To this point, there has been little discussion of clinical issues, specifically, on translating research findings to service delivery contexts. I'll conclude with some personal perspectives on the *why*, *what*, and *how* of these translational needs.

Why Etiologic Classification of SSD?

This chapter's focus on identifying the etiologic causes and clinical signs of subtypes of SSD is essentially similar to the classification perspectives in Duffy's (2005) classic text on motor speech disorders in adults. In his core chapter on differential diagnosis (Chapter 15), Duffy begins with the following quote from Sackett, Haynes, Guyatt, and Tugwell (1991):

> The act of clinical diagnosis is classification for a purpose: an effort to recognize the class or group to which a patient's illness belongs so that, based on our prior experience with that class, the subsequent clinical acts we can afford to carry out, and the patient is willing to follow, will maximize the patient's health. (p. 409)

I obviously agree with Sackett and colleagues and with Duffy on the value of diag-

nostic classification. As suggested at the outset of this chapter, diagnostic classification is required for children with SSD to fully participate in clinical advances in the postgenomic era, including molecular medicine and other new forms of personalized intervention in pre-emptive, prognostic, and targeted treatment applications. For these clinical goals, a systems biology approach seems to me to be the forward-looking framework for classification, rather than, for example, classification typologies based solely on linguistic descriptions or common speech error patterns. On this point, the long-awaited revision of the Diagnostic and Statistical Manual of the American Psychiatric Association, Version V promised for 2011, reportedly is being reorganized to reflect common genomic and other pathobiological backgrounds as the principle classification axes (Helmuth, 2003).

What Topic Areas in SSD Are Most in Need of Programmatic Studies?

Two figures in this chapter have included placeholder boxes for topic areas in SSD that are in need of programmatic study. The first boxes were included in the right arm of the SDCS (see Figure 1–2): "Genetic and Environmental Risk and Protective Factors" and "Neurodevelopmental Substrates." The second and overlapping boxed topics were echoed as later phase research needs in childhood motor speech disorders (see Figure 1–8): "Genetic Substrates and Neural Substrates" and the translational goals of "Assessment, Treatment, and Prevention." Research in all diseases and disorders pursues these public health topics, of course, but only recently have interdisciplinary projects begun to study the genetic, epigenetic, and neurolinguistic substrates of SSD. I would submit that it is time to recast the long-term dichotomy between SSD of unknown (formerly "functional") origin and those of known origin, bringing both together in a consolidated research framework.

Convergence on common genetic, neurodevelopmental, and environmental contributions to typical and atypical speech acquisition should lead to the development of common assessment, treatment, and prevention frameworks. Using an example from research in childhood apraxia of speech, Table 1–3 is a list of complex neurodevelopmental disorders and genetic disruptions in which speakers have been reported to have CAS. As shown in Figure 1–8, we have suggested that such disorders provide a rich source of information on the substrates of CAS, and more generally, of SSD. The descriptions of children's speech in these studies are notably sparse. Most reports continue

Table 1–3. Some Complex Neurodevelopmental Disorders Reporting CAS as a Secondary Sign. Studies are in process for most of the entries in this table.

Autism
Chromosome Translocations
Coffin-Siris syndrome (7q32–34 deletion)
Down syndrome (Trisomy 21)
Rolandic Epilepsy
Fragile X syndrome (*FMR1*)
Joubert syndrome (*CEP290*; *AHI1*)
Galactosemia
Rett syndrome (*MeCP2*)
Russell-Silver syndrome (*FOXP2*)
Velocardiofacial syndrome (22q11.2 deletion)
Williams-Beuren locus duplication (7q11.23)

to appear in medical journals which, understandably, do not include speech phenotype details even if available (although useful phenotypic details are increasingly appearing in on-line supplements). Again, I think it is no longer tenable to compartmentalize SSD research into those of known and unknown origin in the postgenomic era, when advances in understanding and treatment are likely to emerge from and inform one another.

How Can We Best Improve Service Delivery to Children With SSD?

The "how" questions of translational research necessarily involve new skills and technologies, operationalizing them for use in the field. Among the many instrumental approaches that are candidates for the assessment and treatment of children with SSD, skilled use of acoustic techniques (also see Chapters 7 and 8 in this volume), coupled with competence in narrow phonetic transcription seem to offer the highest possibility for widespread clinical accessibility. As described previously, the assessment protocol we use for diagnostic classification requires a laptop computer and masters-level skills in phonetic transcription and acoustic analysis.

A key to the success of the work described in this chapter is the identification and verification of risk factors and diagnostic markers for subtypes of SSD. Table 1–4 is a list of 38 risk factors and diagnostic markers that have been assembled through 2008 for the five proposed subtypes of SD. Some are potential entries for the place markers at the bottom right side of Figure 1–2. The entries in Table 1–4 are preliminary; projects in process are completing validation and cross-validation studies of these and other diagnostic markers with comparison acoustic methods. Taken individually, few of the markers have demonstrated sufficient diagnostic accuracy, which would nominally require that they identify at least 90% of the true positives and true negatives for each subtype. We anticipate using a number of statistical techniques to maximize their combined power to accurately classify children's most likely subtype or composite subtype of SD.

Information such as in Table 1–4, which can be obtained using perceptual and acoustic procedures, should be viewed as reflecting only the current report on this continuing conversation on the causal origins of children's speech sound disorders. Once again, I am profoundly grateful to the many people who have shaped and contributed to the thoughts and findings in this report and to the children and their families who continue to participate in studies with us. More generally, I salute the international community of investigators and clinicians who work daily to help children communicate.

Table 1–4. Sample Perceptual, Acoustic, and Case History Risk Factors and Markers for Five Subtypes of Speech Delay Emerging from Studies Using the SDCS Framework*

Risk Factors and Diagnostic Markers	*SD-GEN*	*SD-OME*	*SD-DPI*	*SD-AOS*	*SD-DYS*
Familial aggregation of any verbal trait (pedigree interview)	+				
Lower language tests scores	+				
Lower nonword repetition task scores (NRT, SRT)	+				
Higher % relative omissions errors (ROI)	+				
Lower % relative sibilant distortion errors (RDI)	+				
Six or more episodes of OME from 0–2 yrs (medical records)		+			
Mean 3–4 freq. thresholds of at least 35 dB on any evaluation (audiological records)		+			
Higher % backing of fricatives (Siblilant Report)		+			
Smaller Intelligibility-Speech Gap (I-S Gap)		+			
Higher % epenthetic vowels on glides (Diacritic Modification Index)		+			
Higher % glottal stop substitutions (DMI)		+			
Higher % nasal-nasal substitutions (Speech Report 1)		+			
Higher % /h/ insertions/substitutions (Speech Report 1)		+			
Higher % initial consonant deletions (Speech Report 1)		+			
Lower first spectral moment on sibilants (<M1)		+			
History of clinically significant psychosocial issues (case records)			+		
Lower scores on psychological/social skills tests (case records)			+		
Lower aggregate speech competence (PCCR, PVCR)			+		
Late (>2 years) onset of speech (case and clinical records)				+	
Late (>6 years) normalization of SD (clinical records)				+	

continues

Table 1–4. *continued*

Risk Factors and Diagnostic Markers	*SD-GEN*	*SD-OME*	*SD-DPI*	*SD-AOS*	*SD-DYS*
Higher % vowel errors				+	
Higher % inconsistent errors on four stability indices				+	
Higher % utterances with inappropriate lexical stress (LSI)				+	
Higher % utterances with inappropriate sentential stress (SSI)				+	
Lower % on Pairwise Variability Index (PVI)				+	
Higher % on Transition Disruption Index (TDR)				+	
Higher % on Syllable Segregation Index (SSI)				+	
Lower ratio on Speech-Pause Index (SPI)				+	
Clinically significant sensorimotor task scores (e.g., tapping rate)					+
Clinically significant oral function task scores (e.g., DDK)					+
Higher % imprecision on Diacritic Modification Index (DMI)					+
Nasal emissions (oral examination; DMI)					+
Smaller planar area for vowels (Vowel Space Index: VSI)					+
Slow articulation and speech rates; by syllable, by phoneme (SRI)					+
Lower Speech Intensity Index (SII)					+
Breathy, strain/strangle; tremulous laryngeal codes (PVSP)					+
Rough voice (jitter, shimmer, harmonics-to-noise ratio) (J, S, HNR)					+
Nasal, denasal, or nasopharyngeal resonance quality (RQA)					+
TOTALS	5	10	3	10	10

*Titles, descriptions, and references for measures and working terms are not included here. Information about most terms can be retrieved using the search function at the Phonology Project Web site: http://www.waisman.wisc.edu/phonology/index.htm .

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