



# The Causal Effects of Genes on Language Disorders across Clinical Conditions

**Written by:** Mabel L Rice, Child Language Doctoral Program/Center for Biobehavioral Neurosciences in Communication Disorders, University of Kansas

**Acknowledgments:** Preparation of this paper was supported by the Merrill Advanced Studies Center at the University of Kansas and grants from the NIH to the University of Kansas through the Mental Retardation and Developmental Disabilities Research Center (P30HD002528), and the following awards to MR: the Center for Biobehavioral Neurosciences in Communication Disorders (P30DC005803), R01DC001803 and R01DC005226.

## Introduction

Language acquisition is an important part of young children's early development. When children's language does not appear when expected or is immature for their ages, they are faced with daunting challenges—they struggle to make themselves understood by their families; they encounter difficulties establishing healthy friendships with other children; and they are likely to experience academic difficulties in school, especially with reading. Above all else, because there is no well-established scientific account of the cause of language impairments, the children and their parents encounter intuitive and often misleading assumptions about causation. People may assume that these children are not trying hard enough to learn language or are intellectually limited. They may also assume that their parents are not expecting them to use language or are not reading or talking enough to their children. Although these assumptions can be well intended, they are often not accurate and can add to the burdens of affected children and their families.

Estimates of the prevalence of children with language impairments vary from study to study, but a good working approximation is 7% for 6-year-old children who do not have other disabilities. The estimate rises to 10% if children with borderline nonverbal intelligence are also included. An additional 1-2% can be added when considering those children who have other disabilities, such as intellectual deficits or conditions such as hearing impairment, autism spectrum, Fragile X, and Williams syndrome. For all children with language impairments the identification of causal agents could move us forward in prevention and intervention, and lessen the great social cost as these youngsters prepare for adulthood and struggle to enter the work place and develop an independent lifestyle.

The scientific challenges of determining the etiology (causes) of language impairment are impressive. First, we do not have a full account of what causes typically developing

children to acquire language so quickly; therefore we cannot start with an established causal mechanism as a place to look for possible differences related to language impairment. Second, language is a complicated system, with multiple dimensions that interact in subtle ways. After decades of detailed inquiry there has been substantial progress in mapping the ways in which various dimensions of language unfold over time in typically developing children. Much less is known about this unfolding in children with language impairments. Even so, it is clear from available evidence that some dimensions of language can be stronger or weaker than others when language impairments exist. This suggests that different dimensions of language may emerge from different causal mechanisms. Instead of a single causal mechanism affecting all dimensions of language equally, multiple causal mechanisms are implicated. Third, language acquisition and language impairments unfold over time, along with other growth phenomena, as children change from toddlers to school-age to adolescents. Reading ability is a later development that becomes closely linked with language impairments and is thought to share underlying causal mechanisms.

At the same time, advances in genetics bring new scientific methods for investigating causal mechanisms. This paper provides a synopsis of current genetics research related to language impairments in children.

### **Key Research Questions:**

- 1) What do the different genotype and phenotypes of language disorders look like?
- 2) What are the linguistic dimensions of affectedness?
- 3) How do we benchmark to the appropriate developmental level?
- 4) How do different clinical populations compare?
- 5) What do genetics studies say about reading, speech and language?
- 6) What do twin studies contribute?

### **Recent Research Findings**

#### ***Genotypes and phenotypes***

Genetic studies focus on the relationship between genotypes (the genetic makeup of an individual) and phenotypes (the observable, measurable characteristics related to individual variations in DNA). Fisher (2006) defines a gene as “a stretch of DNA whose linear sequence of nucleotides encodes the linear sequence of amino acids in a specific protein.” Conventional labels are used to describe locations, such as “7q31” to indicate a location on chromosome 7. Individuals vary in the actual nucleotide sequences. Different persons can have distinctive versions of any particular gene, known as “alleles” or “allelic variants.” At the molecular level, modern genetics aims to determine causal links between the genetic makeup of an individual (genotype) and phenotypic characteristics.

Language impairments, as observable phenotypes, are evident in different clinical populations, each of which has somewhat distinct language characteristics. These populations include children with Specific Language Impairment (SLI), who do not exhibit other developmental disorders, and children with Autism Spectrum Disorder

(ASD), Williams syndrome, Fragile X, or Down syndrome. Genetic causes of the latter three conditions have been identified, although the symptoms of these disorders are complex and extend beyond language impairments to cognitive, social, or physical impairments as well. The known genetic causes of conditions associated with language impairments raise the possibility of comparing across conditions to determine possible genetic sources for differences in language dimensions.

There are two possible approaches. The top-down approach aims for carefully specified phenotypes to aid in the identification of genes affecting language acquisition; the bottom-up approach begins with known genetic syndromes as models of gene effects and aims to identify the language phenotypes. The two approaches are informing current inquiries in a search for gene discoveries that clarify gene effects and possible neurological pathways involved in language disorders.

### ***Linguistic dimensions of affectedness***

Specification of a language phenotype requires differentiation of linguistic and related abilities. Speech is defined as the means through which we communicate language orally, i.e., the sounds we hear individuals produce in telephone communications. Children vary in how easily they learn to speak clearly and intelligibly. A sample of 1,328 children at 6 years of age yielded 3.8% with *speech sound disorders (SSD)* (Shriberg, et al., 1999). SSD may be associated with underlying neurological deficits in the ability to move the articulators, in the form of *oromotor dysfunctions*. Such dysfunctions appear in some clinical groups, although for most children with SSD this difficulty in muscle movements is not evident. In the cases where oromotor dysfunctions are not present, the children are assumed to have unknown difficulties in learning the sound system. SSD are largely independent of other language impairments. Comorbidity of SSD and language impairments at 6 years of age is low. Shriberg et al., (1999) estimate that 1.3% of a sample of 1,328 children show language impairments and SSD. This estimate is from a sample in which all children were assessed, not just those identified as affected with disorders. It is also the case that children with SSD are most likely to be identified as in need of intervention, so they are more likely to be included in clinical caseloads (Tomblin, Records, Buckwalter, Zhang, Smith, O'Brien, 1997).

Children with language impairments may or may not have *general nonverbal cognitive impairments*. Further, children with nonverbal cognitive impairments do not necessarily have language impairments, although it is difficult to identify these children because their limitations usually go undetected. The best available estimate is 11.9% in a large sample of children without other developmental disabilities, where “low cognition” is defined as a nonverbal IQ in the range of 70-87 (Shriberg et al., 1999). In another study with children drawn from the same large sample as Shriberg et al. (1999), Rice et al. (2004) found that the “low cognition” group did not differ from normal controls in general language levels or certain kinds of grammatical ability. Thus, low levels of nonverbal cognition are neither necessary nor sufficient conditions for language impairments.

*Language impairments* can be further differentiated into the components of *vocabulary, morphosyntax, and pragmatics*. Vocabulary refers to children’s word acquisition.

Morphosyntax involves the interface of morphology and word order (syntax) exemplified by sentences such as “Patsy is happy,” “Is Patsy happy?,” and “Patsy will be happy.” These sentences illustrate how the forms of the verb “to be” move to different sites in the clause and change form in different syntactic contexts. Pragmatics involves the social dimensions of language use, including polite forms, story-telling, and conversational interactions.

### ***Benchmarking to expected development***

As children grow older, their language ability increases. Phenotypes suitable for toddlers are not the same as phenotypes appropriate for school age children. Language impairments are conventionally referenced to the levels of ability expected for children’s ages. Thus, technically the definition of language impairment is usually referenced to an arbitrary level of performance for children of the same age, conventionally in the bottom 10-15th percentile. An alternative method used in research is to compare affected children’s performance on a given dimension of language or cognitive performance to a control group of children at equivalent language levels, i.e., younger children at the same general level of language development. This approach allows for determination of the extent to which children’s language disorders are characterized by a general language delay or immaturity, in which the children’s language closely resembles that of younger children, versus the extent to which particular dimensions of language fall further behind a general immaturity. This method can reveal selective deficits, controlling for more general language abilities. It is valuable to differentiate between *language delay*, which is plausibly a matter of immaturity traceable to a delayed emergence of language in toddlerhood, and *language disruption*, characterized by selective deficits in particular dimensions of language (Rice Wexler & Cleave, 1995; Rice & Wexler, 1996; Rice, 2004; Rice & Warren, 2005; Rice, 2007).

### ***Comparing across clinical conditions: Bottom-up and top-down***

An over-arching perspective of the ways in which speech and language impairments appear across clinical conditions was examined by Rice and Smolik (2007). The researchers looked at various speech, language, and cognitive dimensions across clinical conditions in which language impairments appear. The clinical conditions examined included: Specific Language Impairment (SLI), Autism Spectrum Disorder (ASD), Williams Syndrome, Fragile X, and Down Syndrome. The dimensions examined within these clinical conditions included: speech impairment, oromotor dysfunction, cognitive deficit, vocabulary delay, vocabulary loss, morphosyntax disruption, morophosyntax strength, pragmatic deficits, and genetics. The main finding from this comparison was that there was considerable differentiation of speech, language, and cognitive dimensions across the clinical conditions. Speech impairments are more characteristic of children with fragile X or Down syndrome, but, in general, unlikely for children with SLI (although in clinical samples of children with SLI, those with SSD may be overrepresented). Oromotor dysfunction is more evident in children with fragile X or Down syndrome. Cognitive deficits are evident in Williams syndrome, fragile X, and Down syndrome. Vocabulary delays are likely in all the clinical conditions. Documented loss of vocabulary, once word learning begins, is unique to ASD. Morphosyntax can be relatively weak, as in SLI, ASD, and Down syndrome, or relatively strong, as in Williams

syndrome. Pragmatic abilities are relatively intact in SLI and Williams syndrome, but weak in ASD, fragile X and Down syndrome. See Rice and Warren (2004) and Rice, Warren, and Betz (2005) for more detailed descriptions of each clinical condition.

Rice and Smolik (2007) also considered the genetic sources that have been linked to SLI, ASD, Williams syndrome, fragile X and Down syndrome. There is confidence in identified gene sources for Williams syndrome, fragile X and Down syndrome, whereas the chromosome 7 site for SLI is considered provisional and perhaps not characteristic of the most common inherited form of SLI (see Lai et al., 2001; SLI Consortium, 2004), and the chromosome 15 site is one of several currently considered candidates for ASD. The comparison highlights two important points. One is that multiple gene loci are “in play” as potentially contributing to language impairments. The second is that phenotypic and genotypic specifications are not in complete alignment; converging top-down and bottom-up strategies are needed to complete the picture.

### ***Reading, speech, and language***

Genetic investigations of reading impairment are providing important additional clues to the genetics of language impairment. Recent studies report linkage for sites on chromosomes 3, 6 and 15 for persons with reading impairment (Smith, Pennington, Boada & Shriberg, 2005; Stein, et al., 2004; Stein et al., 2006). Linkage is a statistical method of investigating whether the inheritance of any chromosomal interval is correlated (or “linked”) with the inheritance of the trait. These same sites are also linked to phenotypes for phonological short-term memory and SSD in a sample of children with SSD (Smith et al. 2005). In turn, another study investigating persons with SSD phenotype found that affected family members carried a dysfunctional copy of the FOXP2 gene (Shriberg et al., 2006). This genetic anomaly is somewhat different from the findings of Lai et al. (2001) but implicate the same gene. It is likely that more investigations will explore the ways in which the reading, speech, and language phenotypes share common sources of genetic difference.

### ***Twin studies***

Twin studies add to what is known about genetic sources of influence. Monozygotic (Mz, or identical) twins share 100% of their genetic inheritance; dizygotic (Dz or fraternal) twins share about 50%, the same as single-born siblings. Mathematical methods calculate the similarity of co-twins in Mz versus Dz pairs in order to estimate the amount of similarity attributable to genes versus the environment. Studies of twins with language impairments provide a potentially rich way of estimating genetic and environmental influence. Bishop, Adams, and Norbury (2006) studied a sample of 6-year-old twins with language impairments. They reported statistically significant genetic contributions to morphosyntactic and syntactic phenotypes as well as a phonological short-term memory phenotype although the sources were not the same for all three. Their mathematical models predicted a separate source for the phonological short-term memory task. These findings are consistent with the emerging generalization that genetic influences may play out differently across the dimensions of language and related abilities. At the same time, as the previous discussion of the genetics of reading disability pointed out, the same genes can influence multiple phenotypes.

## **Conclusions about genes and environment: A complex interaction**

Determining the genetic contributions of language impairments is a complex undertaking, with a multidimensional array of potential phenotypes, a complicated picture of multiple genes that can act independently or in concert to affect one or more of the phenotypes, and incomplete information on either phenotypes or genotypes of known conditions characterized by language impairment. Although these are early stages of investigation, there is consensus that a single gene as a cause of language impairment is highly unlikely.

There is also widespread agreement that the eventual identification of potential genetic contributions to language impairment will not constitute a deterministic causal model of a given child's language ability. Instead, inherited language aptitude is inherently shaped by interactions with other people in the environment. Parents with high verbal aptitude can pass along that aptitude to their children, for family interactions that are highly verbal in nature provide many opportunities to practice and learn new language skills. On the other hand, parents with lower verbal aptitude or a preference for less talking can pass along those traits for family interactions that are less verbal but nevertheless meet the family's communication needs. Any given family can have a mixture of family members with high-verbal-ability and low-verbal-ability, and most children manage this variation without difficulty as they move toward a robust language competency sufficient for their academic and future workplace needs.

For children with language impairments, the provision of appropriate intervention services can be guided by an awareness of possible intrinsic differences in their aptitude for language acquisition. If there is a history of late language acquisition for other members of the family, young children can be enrolled in early language enrichment programming as a way to prevent later language impairment or to ameliorate any delays in early language onset. Family members and teachers can provide support and encouragement for a young child with language impairments, coupled with patience and acceptance of individual differences as the language system unfolds. Preschool language intervention provides a valuable opportunity for a child's language to develop (cf Rice & Wilcox, 1995). Achievement in reading and other school subjects will benefit from language intervention throughout the school years. In short, enrichment of the teaching environment is our best way to treat language impairments; the era of gene manipulations as treatment is, at best, far in the future. As we learn more about gene and environmental interactions, we will be better able to fine-tune language intervention goals to meet the precise developmental needs of a given child at a particular time (cf., Rice, 2004).

**Date Posted Online:** 2008-06-25 11:30:07

## References

- Bishop, D.V.M., Adams, C.V., & Norbury, C.F. (2006). Distinct genetic influences on grammar and phonological short-term memory deficits: Evidence from 6-year-old twins. *Genes, Brain and Behavior*, 5, 158-169.
- Lai, C.S. et al. (2001). The SPCH1 region on human 7q31: Genomic characterization of the critical interval and localization of translocations associated with speech and language disorder. *American Journal of Human Genetics*, 67, 357-368.
- Rice, M.L. (2004). Growth models of developmental language disorders. In M.L. Rice and S.E. Warren (eds), *Developmental language disorders: From phenotypes to etiologies* (pp 207-240). Mahway, NJ: Erlbaum.
- Rice, M.L. (2007). Children with specific language impairment: Bridging the genetic and development perspectives. In E. Hoff and M. Shatz (Eds.), *Handbook of language development* (pp 411-431). Cambridge, MA: Blackwell.
- Rice, M.L., & Smolik, F. (2007). Genetics of language disorders: Clinical conditions, phenotypes, and genes. In Gaskell, M.G. (Ed.) *The Oxford handbook of psycholinguistics* (pp. 685-700). Oxford, England: Oxford University Press.
- Rice, M.L., Tomblin, J.B., Hoffman, L., Richman, W.A., & Marquis, J. (2004). Grammatical tense deficits in children with SLI and nonspecific language impairment: Relationships with nonverbal IQ over time. *Journal of Speech, Language, and Hearing Research*, 47, 816-834.
- Rice, M.L., & Warren, S.E. (2005). Moving toward a unified effort to understand the nature and causes of language disorders. *Applied Psycholinguistics*, 26, 3-6.
- Rice, M.L., Warren, S.E., & Betz, S.K. (2005). Language symptoms of developmental language disorders: An overview of autism, Down syndrome, fragile X, specific language impairment, and Williams syndrome. *Applied Psycholinguistics*, 26, 7-28.
- Rice, M.L., Wexler, K., & Cleave, P..L. (1995). Specific language impairment as a period of extended optional infinitive. *Journal of Speech, Language, and Hearing Research*, 38, 850-863.
- Rice, M.L., & Wexler, K. (1996). Toward tense as a clinical marker of specific language impairment in English-speaking children. *Journal of Speech, Language & Hearing Research*, 39, 1239-1257.
- Rice, M.L., & Wilcox, K. A. (1995). *Building a language-focused curriculum for the preschool classroom: A foundation for lifelong communication*. Baltimore, MD: Paul H. Brookes Publishing.
- SLI consortium. (2004). Highly significant linkage to the SLI1 locus in an expanded sample of individuals affected by specific language impairment. *American Journal of Human Genetics*, 74, 1225-1238.
- Smith, S.D., Pennington, B.F., Boada, R., & Shriberg, L.D. (2005). Linkage of speech sound disorder to reading disability loci. *Journal of Child Psychology and Psychiatry*, 46, 1057-1066.
- Shriberg, L.D. et al. (2006). Speech, prosody, and voice characteristics of a mother and daughter with a 7;13 translocation affecting FOXP2. *Journal of Speech, Language, Hearing Research*, 49(3), 500-525.

- Shriberg, L.D., Tomblin, J.B., & McSweeney, J.L. (1999). Prevalence of speech delay in 6-year-old children and comorbidity with language impairment. *Journal of Speech, Language, and Hearing Research, 42*, 1461-1481.
- Stein, C.M., Millard, C., Kluge, A., Miscimarra, L.E., Cartier, K.C., Freebairn, L.A., et al. (2006). Speech sound disorder influenced by a locus in 15q14 region. *Behavioral Genetics, 36*(6), 858-68.
- Stein, C.M., Schick, J.H., Gerry Taylor, H., Shriberg, L.D., Millard, C., Kundtz-Kluge, A., et al. (2004). Pleiotropic effects of a chromosome 3 locus on speech-sound disorder and reading. *American Journal of Human Genetics, 74*(2), 283-297.
- Tomblin, J.B., Records, N.L., Buckwalter, P., Zhang, X., Smith, E., & O'Brien, M. (1997). Prevalence of specific language impairment in kindergarten children. *Journal of Speech, Language & Hearing Research, 40*(6), 1245-1260.

To cite this document:

Rice, M.L. (2008). The causal effects of genes on language disorders across clinical conditions. *Encyclopedia of Language and Literacy Development* (pp. 1-8). London, ON: Canadian Language and Literacy Research Network. Retrieved [insert date] from <http://www.literacyencyclopedia.ca/pdfs/topic.php?topId=244>