

Pedigree Analysis of SLI And Related Disorders in a Multigenerational Family

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Abstract

A pedigree analysis was performed for a 50 member, multigenerational family ascertained for an SLI proband. Rates of impairment for language, reading, spelling, and rate processing were examined. In addition, composite affectation rates of impairment obtained through direct testing were compared to rates of impairment obtained through history questionnaire data. Results: Individual phenotypic impairment rates ranged from 22-34%. Although composite affectation rates and rates from history data were both high, there was some variability in the identification of affected individuals. Furthermore, several family members expressed more than one type of impairment supporting the notion of co-occurrence of these disorders. Pedigrees of both composite affectation rate and questionnaire data reflected transmission patterns consistent with an autosomal dominant mode of transmission.

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Introduction

Both oral and written language impairments aggregate in families and in many cases co-occur in the same individuals (Flax et al., 2000). To date, gene-linkage studies have identified significant linkage for dyslexia (Fischer et al., 1999; Gayan, et al., 1999) and most recently for speech and lan-

guage in conjunction with severe oral motor dyspraxia (Lai et al., 2001). However, identification of specific genes for specific language impairment (SLI) have yet to be reported. Case studies, case-control family studies, family questionnaire reports, and extended family studies have all been used to determine familial rates of impairment. Twin studies (Bishop et al., 1995) as well as analyses of extended families (Bartlett et al., 2001) have been used for estimating the heritability of language and reading. Precursors for gene-linkage studies are pedigree analyses which can provide useful information about likely modes of transmission (i.e. autosomal dominant, common recessive) and provide information regarding the underlying genetic liability. The advantage of looking at one large extended family rather than a series of smaller pedigrees (as in segregation analysis) is that behavior segregating in a single family is more likely to have a single underlying genetic basis. Here we report on a large multi-generational family ascertained through an SLI proband.

Rationale

Complex disorders such as SLI and dyslexia do not follow simple Mendelian inheritance patterns. Variable expressivity may be evident with the same underlying deficits expressed differently in different people and changing over time (Conti-Ramsden et al., 1999), further complicating the identification of any simple mode of inheritance. In addition, multiple deficits may co-occur within the same individual (Flax et al., under review).

Aims

- 1) To examine the language, reading, spelling, and perceptual skills, based on current test data, of a large multigenerational family with a positive history for SLI by looking at:**
 - a. individual phenotypic classifications,**
 - b. rates of impairment,**
 - c. combinations of phenotypes for determining more global affectation rates,**
 - d. possible modes of transmission.**

- 2) To examine the changing profiles of family members over the lifespan by comparing current test data to family history data.**

Subjects

As part of a large genetic linkage study, a pedigree was developed for a 50 member multigenerational family with an identified SLI proband. A comprehensive battery of standardized and experimental language, reading, spelling, and perceptual measures was administered to 45 of the members who were available for testing and 46 filled out a comprehensive questionnaire documenting their language and learning development. One family member was deceased but several surviving family members reported a history of reading problems for this person.

Methods

Language Impairment (LI)

- Spoken Language Quotient ≥ 85 on age-appropriate version of Test of Language Development (TOLD)
or
- Mean of TOLD and Token Test* score ≥ 85
or
- Mean Subtype score ≥ 7 in two or more language subtypes (receptive, expressive, or grammar from TOLD composite scores)

Reading Impairment (RI)

- A standard score ≥ 85 on one or more of the following subtests of the Woodcock Reading Mastery Test-Revised:
 - Word Attack
 - Word Identification
 - Passage Comprehension

Spelling Impairment (SI)

- A standard score ≥ 85 on the age appropriate Spelling subtest of the Wide Range Achievement Test (WRAT)

Rapid Auditory Processing Impairment (RAPI)

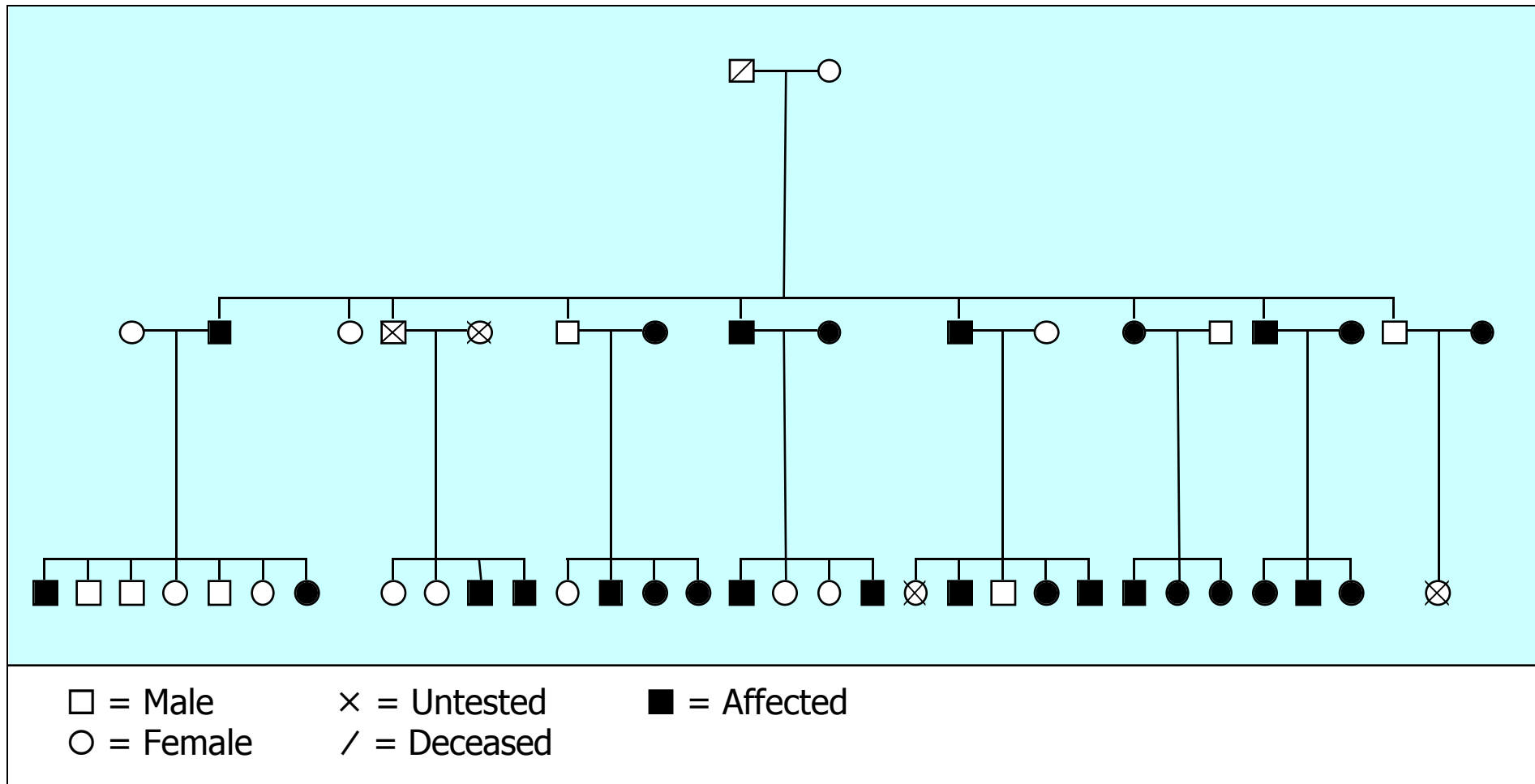
- Passed hearing screening
and
- Received $\geq 65\%$ on the auditory rate processing subtests of the Tallal Repetition Task**

Language/Learning History (HX)

- **ADULTS:** considered affected if reported history of language or reading problems or received help in school for language, articulation, or reading.
- **CHILDREN:** considered affected if parents reported that they had current or past problem in language, speech, or reading development and/or if they received special help for these problems in school.

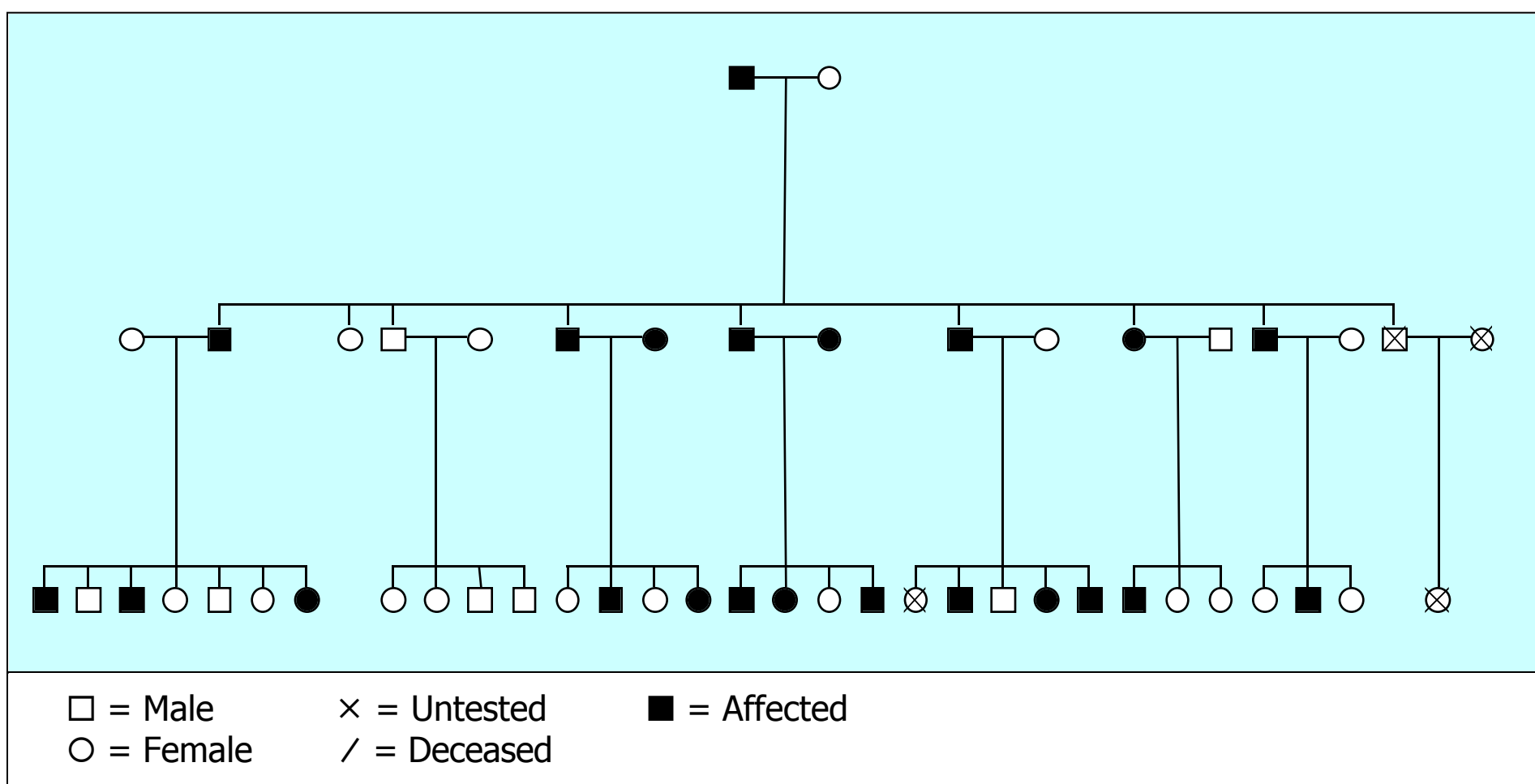
Results

Pedigree Based on Current Testing: Overall Affection Status



- **Affection rate (27/45) = 60%**
- **Consistent with autosomal dominant mode of transmission**

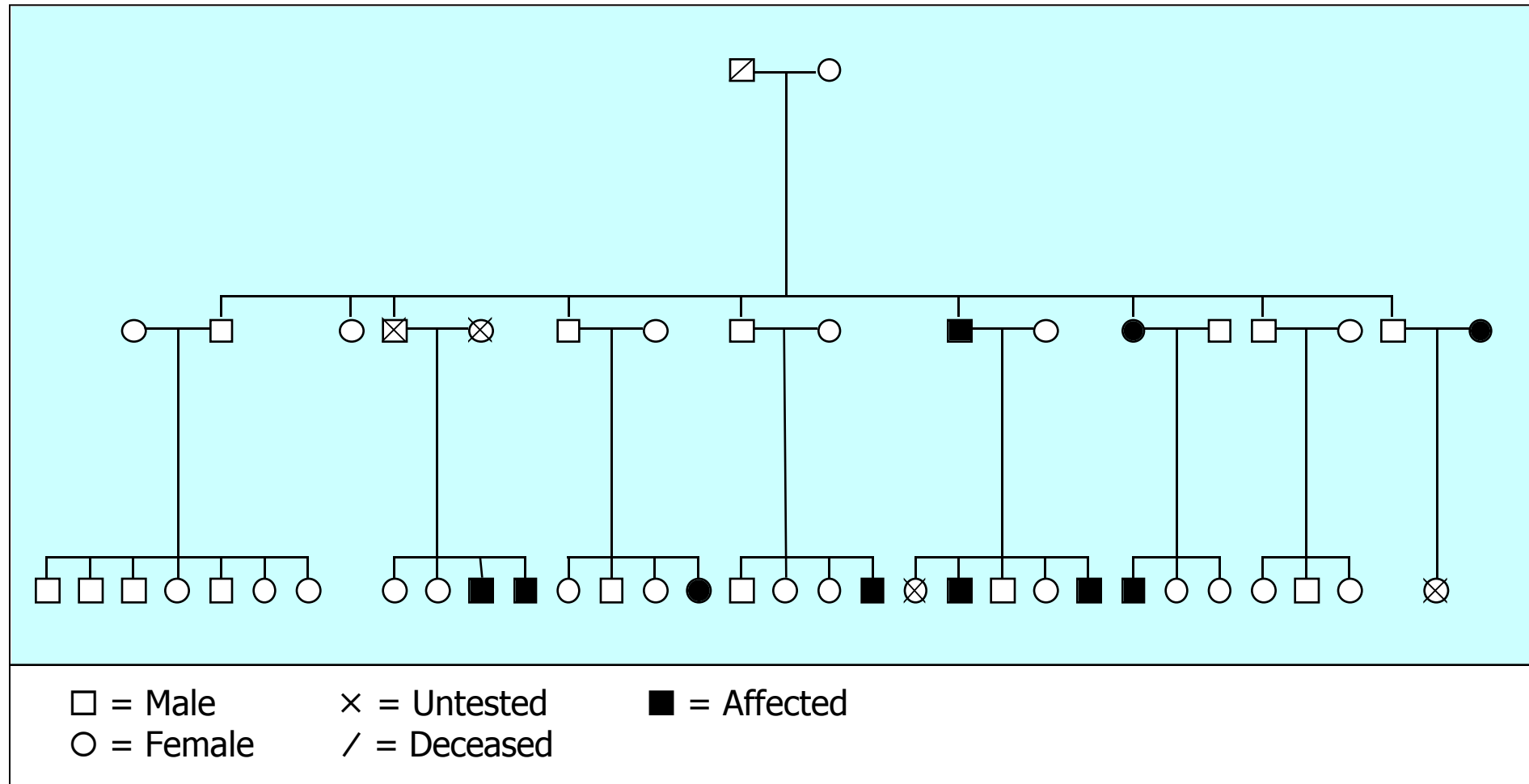
Pedigree Based on Family History Questionnaire



- **Affection rate (22/46) = 48%**
- **Consistent with autosomal dominant mode of transmission**

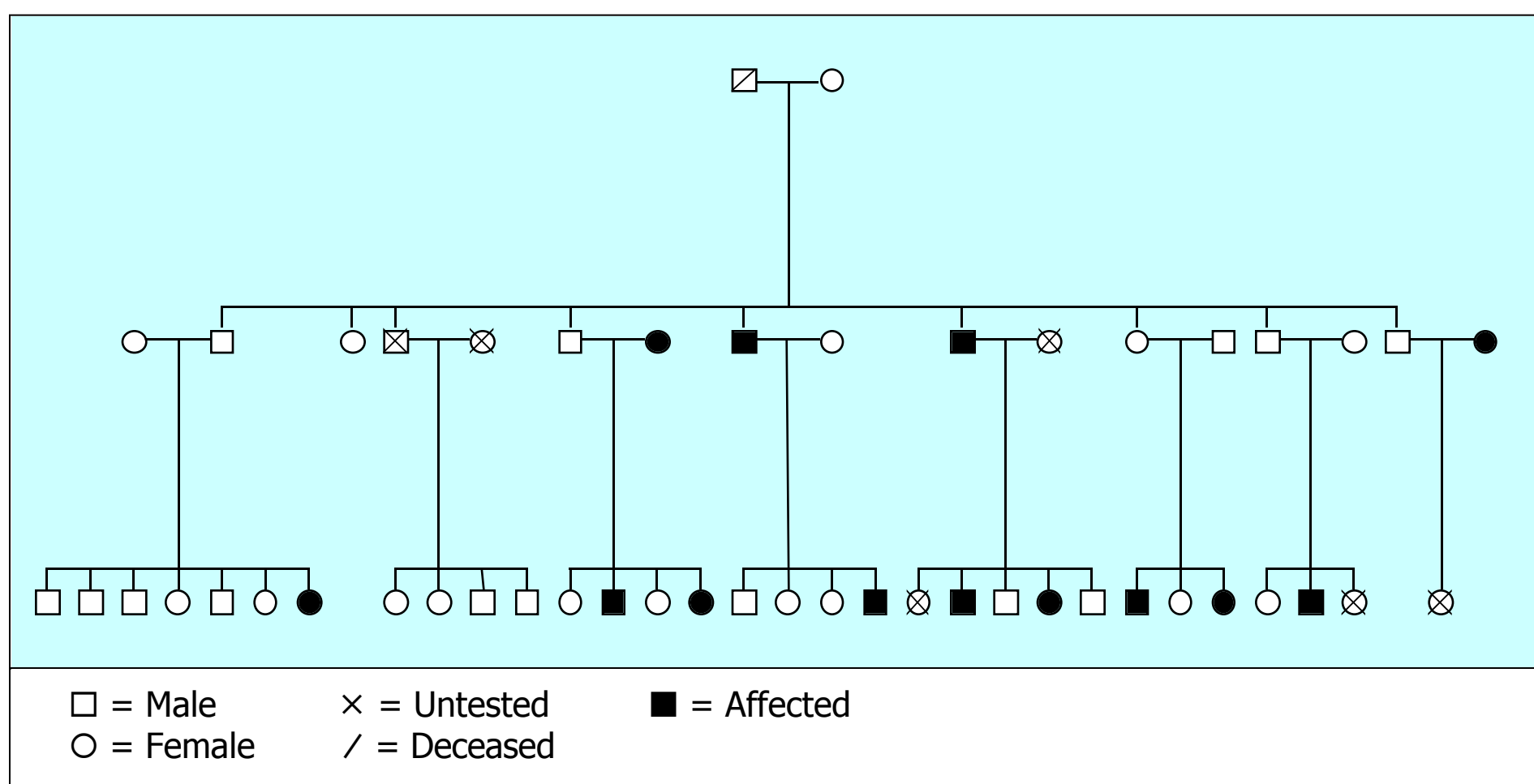
Rates of impairment are high using both methods. However, closer inspection reveals that current test scores and family history questionnaires do not always identify identical subsets of individuals.

Pedigree Based on Language Impairment (LI) Phenotype



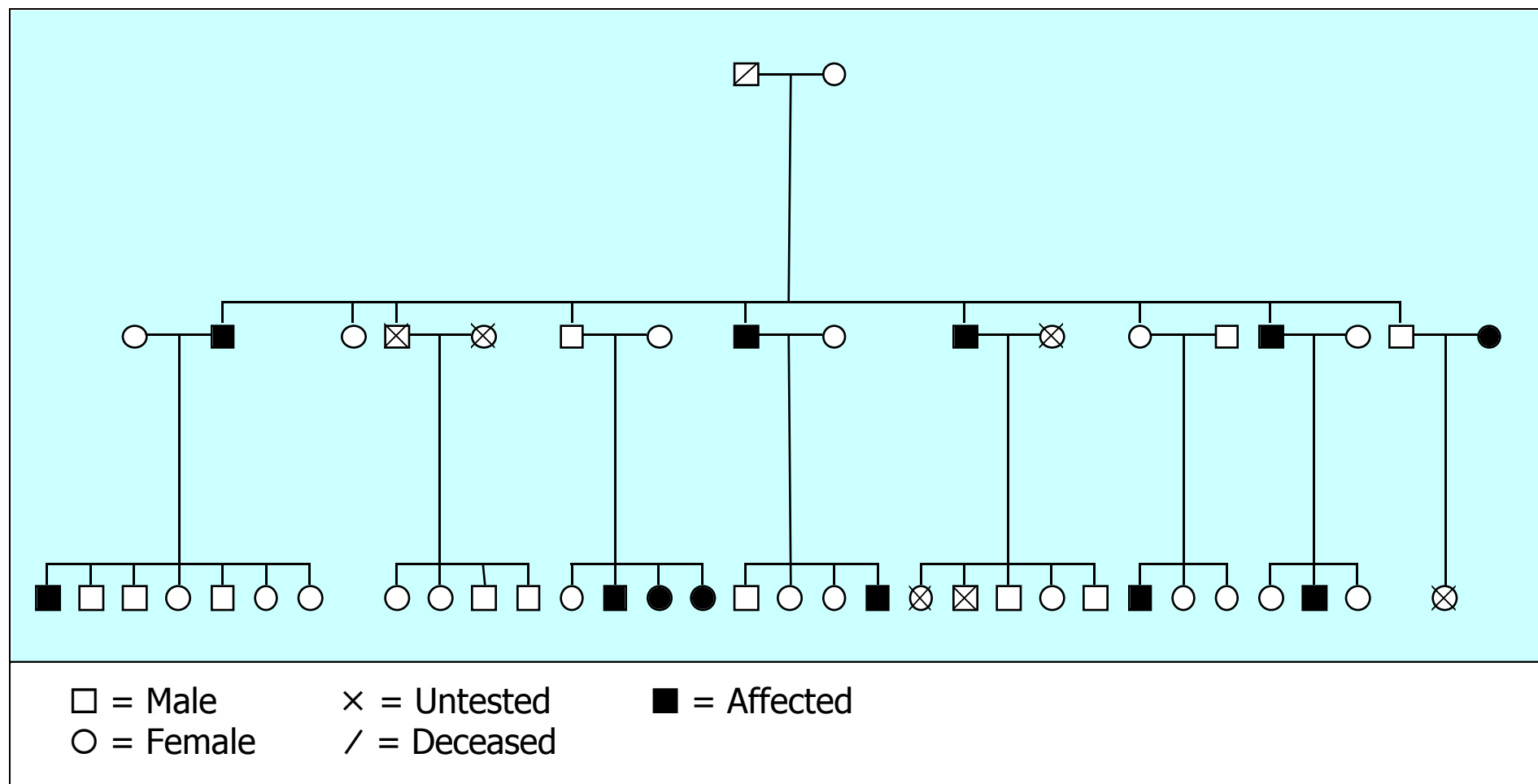
• **Affectation rate (10/45) = 22%**

Pedigree Based on Reading Impairment (RI) Phenotype



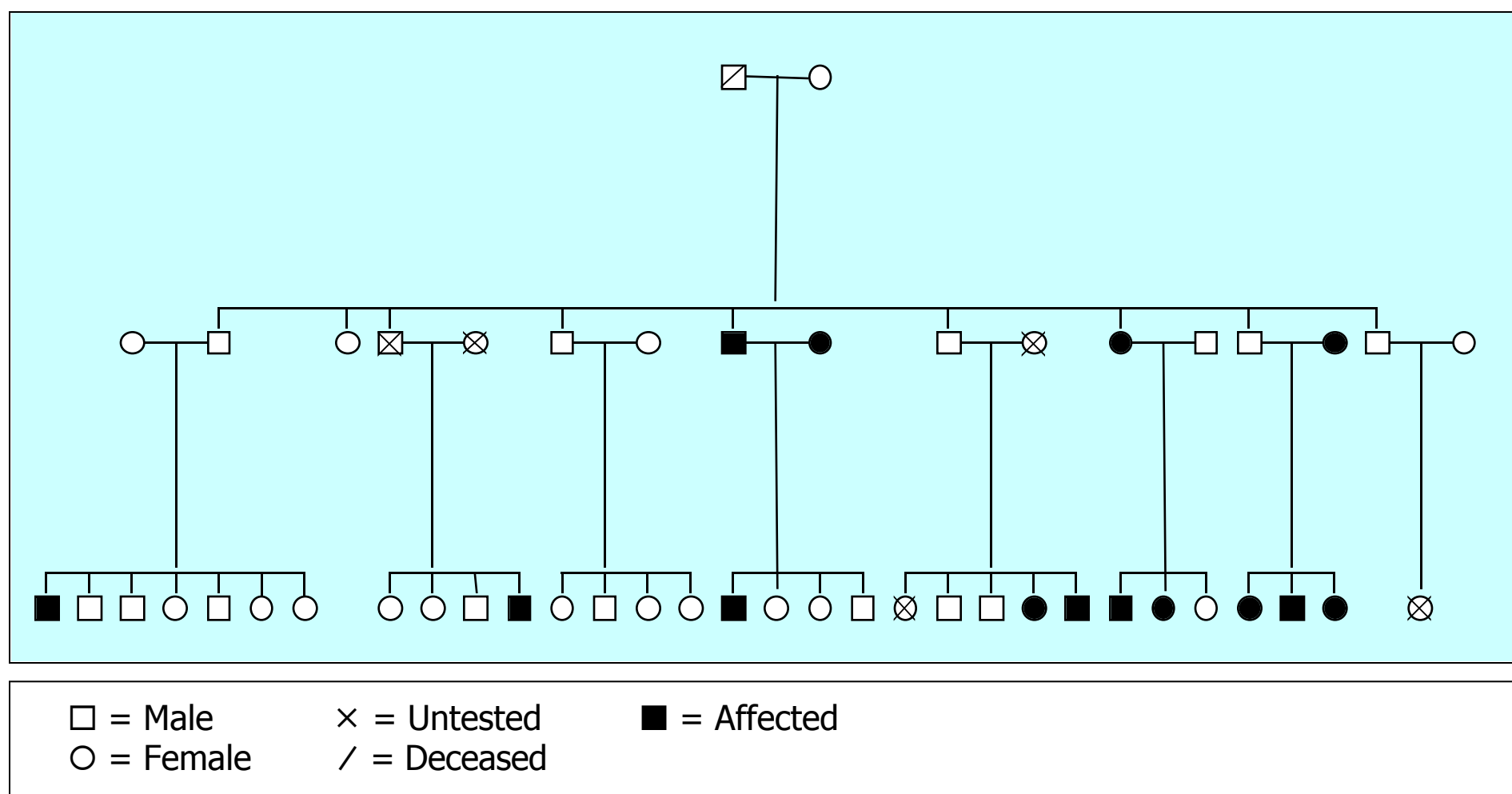
• **Affectation rate (13/43) = 30%**

Pedigree Based on Spelling Impairment (SI) Phenotype



- **Affectation rate (12/43) = 28%**

Pedigree Based on Rapid Auditory Processing Impairment (RAPI) Phenotype

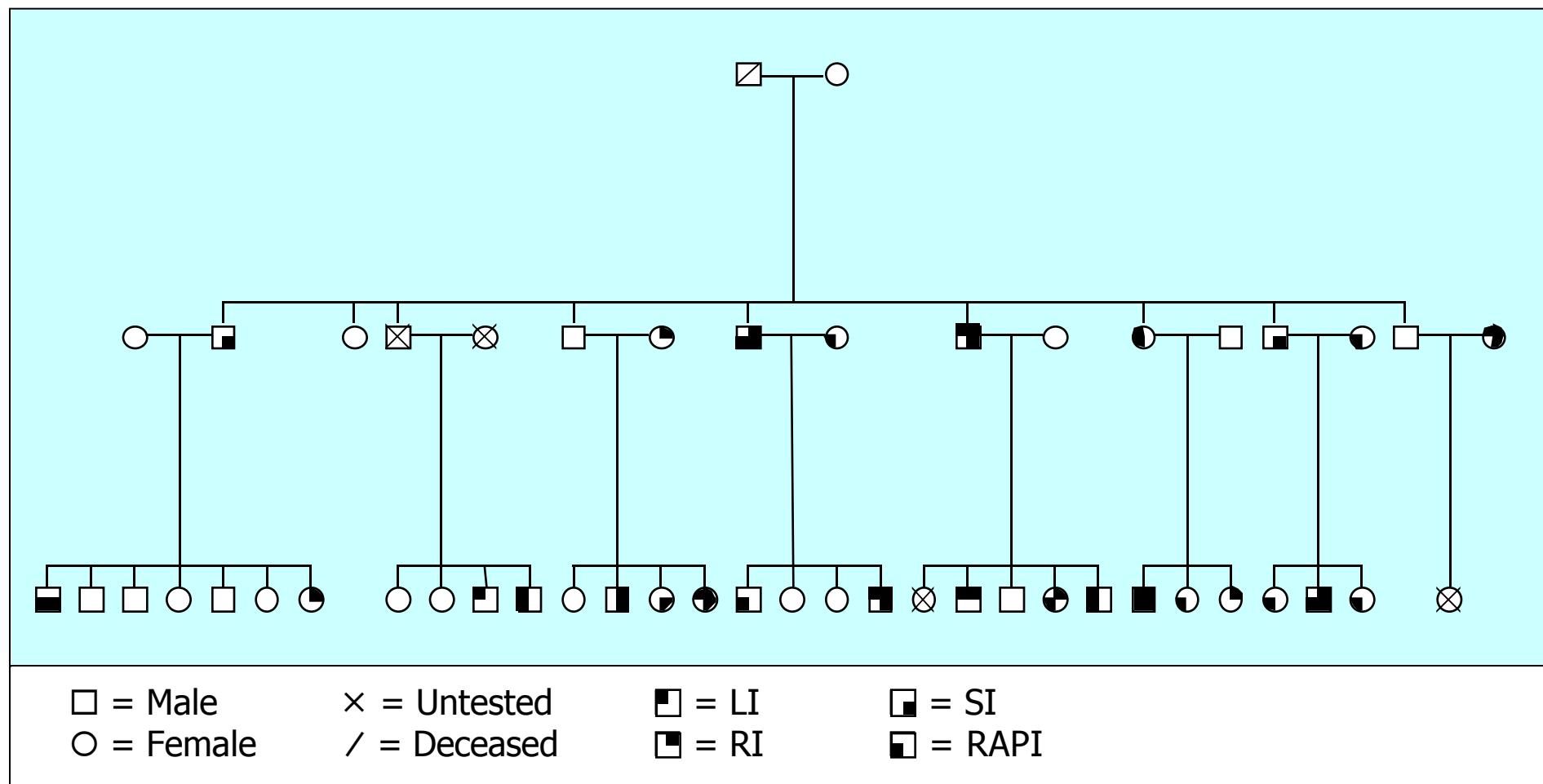


- **Affectation rate (14/44) = 32%**

Variable expressivity and changes over the lifespan (i.e. LI being more prevalent in children than adults) most likely con-

tribute to difficulty in identifying more of transmission when looking at more specific phenotypes.

Co-occurrence of LI, RI, SI, and RAPI



Several family members exhibit more than one type of language/learning impairment, supporting the notion that these types of disorders co-occur within individuals.

Summary

Affectation rates reflect variable expressivity: different family members presented with related but different phenotypic profiles. This made predictions about modes of transmission difficult. Individual phenotypic rates of impairment ranged from 22-34%.

Lifespan issues were reflected in the fact that LI was more prevalent in children than adults and that history information

reflected the greatest number of affected family members.

Affectation rates from current testing and history questionnaire data were both high. However, close inspection of the data demonstrated that these two methods of classification may identify different individuals (Tallal et al., 2001).

Several family members expressed more than one type of impairment supporting the notion of co-occurrence of these disorders (Flax et al., under review).

An examination of composite pedigrees from current testing or history data from those who completed the questionnaire, revealed transmission patterns consistent with an autosomal dominant mode of transmission.

In this family there were instances of both parents being affected. Although a very interesting phenomenon that could reflect sociological and socio-economic issues, it made predicting the mode of transmission more difficult.

Conclusions

Pedigrees can be a useful first step in preparing data for linkage analysis and heritability studies.

A combination of history and current status should be used for identifying oral and written language phenotypes since finding specific phenotypes for SLI or dyslexia are often clouded by lifespan issues.

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Notes

* Tomblin, Freese and Records (1992) administered an adapted version of the Token Test for Adults (DeRenzi & Vignolo, 1962; DeRenzi & Faglioni, 1978) to 70 adults; 35 who had been diagnosed as LI and 35 who had not. Within each of these two groups of adults, percentage scores on the Token Test were normally distributed. It was found that one standard deviation below the mean of the control group corresponded to one standard deviation above the mean for the language impaired group, indicating that this test is able to distinguish between language impaired and normal adults. This information was used to translate scores on the Token Test from the current study, expressed as percent correct, into standard scores with a mean of 85 and a standard deviation of 15.

** Tallal Repetition Test consists of 2 tone and 3 tone sequences presented rapidly in succession at 75 msec tone durations, at 100 and 300 Hz, presented with ISIs of 10 and 70 msec (Tallal & Piercy, 1973 a&b).