UNEXPECTED SEX-RATIOS IN FAMILIES OF LANGUAGE/LEARNING-IMPAIRED CHILDREN*

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Abstract—There is a well-documented propensity of males affected with developmental language/
learning impairment. Results from this study demonstrate, unexpectedly, that this sex-ratio difference
of males to females with developmental language/learning disorders was found to occur significantly
only in families with a language/learning-impaired mother. In addition, a remarkably aberrant
offspring sex-ratio was found in families of language/learning-impaired children who had an affected
mother, but not father. Mothers who were developmentally language/learning-impaired had three
times as many sons as daughters, and five times as many language/learning-impaired sons as
daughters. Genetic and hormonal influences that might affect both sex-ratio and neuroanatomical
development and disorders are discussed.

INTRODUCTION

THE PREVALENCE of developmental language disorders in children has been reported to be between 8–15% of all preschool-aged children, with a higher 2–3:1 ratio of boys to girls affected [1, 3, 24, 45]. Based on this increased incidence of boys to girls affected, and the finding of significant family aggregation in first-degree relatives of language-impaired children, [4, 19, 40, 50] sex-linked modes of genetic transmission have been postulated as a possible etiology for some specific developmental language impairments [24].

One approach to the study of a possible sex-linked mode of genetic transmission for language impairment has been to follow, prospectively, children with known sex-chromosome abnormalities and assess them for development of language difficulties. Studies of language development in aneuploid children (45 X , 47 XYY, 47 XXY, and 47 XXX) have been reported [25, 29, 30, 32, 36, 38, 39, 42, 54]. These studies have found that of these children, those with an additional X chromosome show a significantly increased frequency of delayed language development. PUCK *et al.* [38] also studied the speech development of 47 XXY boys and reported that they showed a lag in speech development. NIELSEN and SILLESEN [31] and ROBINSON *et al.* [41] also studied 47 XXY boys and reported an increase in frequency of language difficulties. However, neither of these studies specified the type or degree of speech or language deficit, and the authors failed to provide any objective speech or language test results to support their conclusions.

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GRAHAM et al. [16] and STEWART et al. [47] report well-controlled, objective studies of language, reading, spelling, and memory abilities of 47 XXY boys. GRAHAM et al. [16] demonstrated significant reductions in verbal, but not performance IQ, expressive language dysfunction, and reading and spelling disabilities for the XXY group. Further evaluation also demonstrated significant deficits in both non-verbal and verbal auditory processing and memory abilities for the XXY group. Findings of verbal and memory deficits in XXY boys are also reported by STEWART et al. [47] These findings are particularly significant due to their strikingly similar pattern of deficit in language, as well as non-verbal and verbal processing and memory, to that reported by TALLAL and PIERCY [48, 49] and TALLAL et al. [51, 52] for children with specific developmental language/learning impairment of unknown origin (developmental dysphasia).

Females with an additional X chromosome (XXX) have also been reported to have receptive language problems [36] and lower verbal IQ [32]. These authors point out, however, that the language problems are difficult to evaluate, and probably not specific, due to generalized cognitive deficiencies in these subjects.

Addressing the question from the opposite perspective, children with developmental language disorders have been tested for sex-chromosome abnormalities. Several authors report an increased frequency, as compared to the normal population, of sex-chromosome abnormalities in children with delayed language acquisition [11, 13, 26]. Unfortunately, these studies have been criticized because subject selection criteria were not made explicit; no attempt was made to select for specific language disorders, to confirm a diagnosis of language delay, or even to rule out other possible diagnosis [56]. Thus, although these results are intriguing, no firm conclusions can be drawn from these data.

Another approach to investigating whether a sex-linked mode of genetic transmission might be a possible etiology for some specific developmental language disorders is to evaluate family history data. Several case reports of families with several members having language disorders support a possible genetic etiology [2, 5, 28, 43]. Similarly, group studies of language-impaired children report family aggregation of language/learning problems [4, 40, 50]. However, none of these studies have addressed issues pertaining to sex-linked modes of genetic transmission.

The purpose of this study was to determine if the pattern of family history data obtained from a large, empirically-defined population of children with specific developmental language disorders (developmental dysphasia) would lend support to any known modes of sex-linked genetic transmission.

METHODS

Subjects

Sixty-two, 4-yr-old, specifically language-impaired children participated as subjects in this study. These subjects represented approx 75% of the language-impaired subjects participating in the San Diego Longitudinal Study of language impairment for whom family history data on both biological parents and all siblings was available. In order to ascertain as homogeneous and well-defined a sample as possible, each child had to meet all of the following criteria to be included as language-impaired: (1) age 4.0–4.11 at time of induction; (2) a non-verbal performance IQ of 85 or better on the Leiter International Performance Scale; (3) a mean language age (when computed from standardized expressive and receptive scores) at least 1 yr below both performance mental age and chronological age; (4) normal hearing acuity, no motor handicaps, no oral, structural, or motor impairments affecting non-speech movement of the articulators; (5) an English language background without signficant dialectical or language differences in the home environment; (6) no obvious signs of infantile autism (as defined by DSM-III, 1980); and (7) no neurological disorders (seizure disorder, hemiparesis, etc.).

The majority of the language-impaired subjects had both severe expressive and receptive language deficits,

although some were more severely impaired receptively, while others had a more severe expressive language disorder. Over (60%) also had a speech articulation impairment. However, children with articulation deficits alone, without language disorders, were not included in the study.

Family history data

At the time of induction into the longitudinal study, the biological mother and father of each subject were each requested to fill out a separate questionnaire, relating to family history of language, reading, writing, and academic achievement. This questionnaire comprised 35 detailed questions adapted from questionnaires used previously by CHILDS and FINUCCI [6] and KIDD [22] to investigate familial aggregation in other communicative disorders. Because of the lack of good diagnostic criteria when the parents were children, and because of the relationship between language disorders and subsequent academic achievement, particularly reading and writing, *parents* were classified as "affected" if any of the following were reported:
(1) a history of language problems;
(2) a history of below-average school achievement, to the eighth grade, in reading, writing, or both;
(3) a history of ever having been kept back a grade in school, through the eighth grade.
Considerable help was given to parents filling out these questionnaires, including written descriptions, explanations and examples of technical terms such as "expressive language" etc., to aid them in making accurate judgements. Questionnaires were only accepted if filled out directly by each biological parent. Questionnaires were filled out initially by the parent and then reviewed together with a research assistant, so that questions could be resolved. Every effort was made to assure that questionnairies were completed and returned, and were accurate.

Sibling classification was somewhat more problematic. In the original questionnaire, we inadvertently failed to either (1) clarify whether proband–sibling relationships were on full- or half-sibs, or (2) specify sex of siblings. The latter information is of interest, and the former information is imperative to accurately assess familial impairment frequencies. Parents were recontacted by telephone or mail to obtain these additional sibling data. Combining questionnaire and telephone data, information was available on all primary relatives (both biological parents and all full-sibs) on 62 impaired probands. Siblings were diagnosed as "affected" if parents reported for them a positive history for difficulties in reading, writing, language, or other learning disabilities.

Due to the young age of the subjects in the study, siblings also tended to be young. Because of this, subclassification of siblings by type of impairment was impossible (e.g. many sibs had not yet reached school-age when reading and writing deficiencies might first become apparent). Therefore, sibs were classified as either "affected" or "not affected" without further differentiation. It must be kept in mind that, because of the young age of many of the siblings, results may under-represent the actual number of eventually affected sibs.

RESULTS

The 62 language-impaired children consisted of 44 males and 18 females for a 2.4:1, male:female ratio, correlating well with previously reported population frequencies [3, 24, 45]. The language-impaired children were all 4 yr old (mean 4.4 ± 0.3) and had a mean non-verbal IQ of 108 ± 12, as measured by the Leiter International Performance Scales. Their language abilities, as measured by standardized speech and language tests, ranged from 2.6 to 4.1 (mean 3.2 ± 0.4) yr on receptive language tests and 2.7 to 3.7 (mean 3.0 ± 0.2) yr on expressive language tests, demonstrating that they were, on average, $1-1\frac{1}{2}$ yr delayed in language development.

Parental data

Table 1 shows, for language-impaired probands, the relationship between the proband's sex and parental impairment. For the language-impaired boys, 23% had both parents affected, 18% had only an affected mother, and 25% had only an affected father. Of the 44 language-impaired boys in the study, 66% had an affected parent. For language-impaired girls, 11% had both parents affected, 11% had only a mother affected, and 33% had only a father affected. Of the language-impaired girls 55% had an affected parent. There was no statistically significant difference between the number of language-impaired boys and girls with or without an affected parent ($\chi^2 = 0.59$, ns). Combining language-impaired girls and boys, 39 (63%) of the probands report at least one affected parent.

TABLE 1. Sex of affected parent by sex of impaired proband

N	Both affected	Mother affected	Father affected	Neither affected
Male (44)	10 (23%)	8 (18%)	11 (25%)	15 (34%)
Female (18)	2 (11%)	2 (11%)	6 (33%)	8 (45%)

The number and percentage of language-impaired males and females that have both parents affected, mother but not father affected, father but not mother affected, or neither parent affected are shown. $N =$ the total number of male and female language-impaired probands in the study.

In order to determine whether the sex of the proband is associated with the sex of the affected parent, only families with one affected parent were used (i.e. affected mothers having offspring with non-affected fathers and vice versa). To minimize confusion as to the source of impairment, families with both an affected father and mother were not used for these analyses. For those language-impaired probands with only one affected parent, no significant association was demonstrated between the sex of the proband and sex of the affected parent ($\chi^2 = 0.16$, ns). Within the group of language-impaired children without an affected parent, although there were more boys than girls, this difference was not significantly different from the expected 1:1 sex-ratio in the general population (15 boys, 8 girls; 1.9:1 ratio, $\chi^2 = 2.1$, ns). However, within the group of language-impaired children who did have an affected parent, there were almost three times as many boys as girls (29 boys, 10 girls; 2.9:1 ratio), a highly significant ratio difference ($\chi^2 = 9.3$, $P \leq 0.01$). Although the ratio of LI boys to girls is higher in the group with an affected parent (2.9:1) than it is in the group without an affected parent (1.9:1), the difference between these groups does not reach statistical significance ($\chi^2 = 0.59$, ns).

Sibling data

The LI boys had 48 brothers and 23 sisters, while the LI girls had 17 brothers and 12 sisters. In order to determine whether the sibling sex-ratio was significantly different for LI boy vs LI girls, the number of sisters was subtracted from the number of brothers for each LI proband. These differences were rank ordered and compared using a Mann–Whitney U test, which showed no significant between-group difference ($P = 0.70$, ns). Table 2 shows, for language-impaired probands, the relationship between the sex of impaired probands and the sex and impairment rates of their siblings. For the language-impaired boys, 17 (35%) of their brothers and 6 (26%) of their sisters were also affected. For the language-impaired girls, 10 (59%) of their brothers and 5 (42%) of their sisters were also affected. There was no significant difference between the number of language-impaired boys and girls with affected siblings ($P = 0.70$, ns). Thus, the sex of the proband is not significantly associated with either the impairment rate or sex of their affected siblings.

Family data

Figure 1 shows the relationship between the number of affected parents and the number of affected siblings (not including proband), with the distribution into groups being based on the presence or absence of either affected mother or father. For both the affected and non-affected fathers, 38% of their offspring were affected. Thus, for the fathers, there is no difference between their number of affected vs non-affected offspring, based on whether they themselves were affected or non-affected ($P = 0.82$, ns). For mothers of language-impaired

TABLE 2. Sibling impairment rates and sex by sex of impaired proband

Proband sex	Number	Affected male sibs	Affected female sibs	Total affected sibs
Male	44	17/48 (35%)	6/23 (26%)	23/71 (32%)
Female	18	10/17 (59%)	5/12 (42%)	15/29 (52%)

The rate (number of affected siblings/total number of siblings), percentage, and sex of affected siblings are shown separately for the language-impaired boys and girls.

children, half (51%) of the offspring (excluding proband) of affected mothers were affected, whereas only 31% of the offspring of non-affected mothers were affected. Although affected mothers show a trend towards having more affected offspring than do non-affected mothers, differences between these groups approached, but did not reach, statistical significance ($P = 0.17$, Mann–Whitney U test).
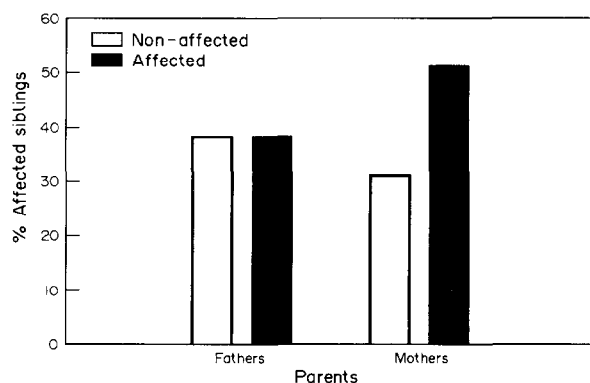

FIG. 1. The percentage of affected offspring (excluding proband) are shown for affected vs/non-affected fathers and mothers.

Sex-ratios

In the general population, there are roughly equal numbers of boys and girls born [53]. It was, therefore, unexpected to find that the language-impaired probands had almost twice as many brothers as sisters. As can be seen in Table 2, the language-impaired children had 65 brothers but only 35 sisters, a 1.9:1 ratio. In terms of absolute numbers of offspring, affected fathers had only slightly more male than female offspring (not including probands: 23 and 17 respectively; 1.4:1 ratio). However, affected mothers had two-and-a-half times as many sons as daughters (25 boys and 10 girls, a ratio of 2.5:1). To better specify the contribution of the sex of the affected parent to offspring sex-ratio, families with only one affected parent (i.e. affected fathers having offspring with non-affected mothers, and vice versa) were analyzed. The proportion of male to female offspring was calculated for all families with only one affected parent. A t-test analysis of the arcsin of the proportion of male to female children for affected fathers vs affected mothers demonstrated a statistcally significant between-group difference ($t = 2.2$, $P < 0.03$).

Figure 2 shows the sex-ratio of offspring aggregated by the number and sex of affected parent (neither parent affected, affected mother but not father, affected father but not mother, and both parents affected). Sex-ratios were calculated for (a) all offspring, including

probands, (b) only affected offspring, excluding proband, and (c) affected offspring, including proband. As can be seen in Fig. 2, families with neither parent affected had offspring sex-ratios of 2:1 or less. However, families with both parents affected had male:female offspring ratios of 2.8–4.3:1. When families with an affected father and a non-affected mother were examined, the offspring sex-ratio was found to approach that expected in the normal population, 1–1.6:1. When families with only an affected mother and a non-affected father were examined, a highly aberrant sex-ratio was found. These mothers had a consistently higher number of male to female offspring: a sex-ratio of 3.5:1 was found when all offspring, including probands were examined; the sex-ratio increased to 5.3:1 for affected offspring, including probands; and when probands were excluded in calculations of affected offspring, affected mothers had eight times as many male as female offspring. To determine whether the sex-ratio of affected offspring was significatly different, depending on the sex of the affected parent, the mean proportion of affected male to female offspring was calculated. The mean proportion of affected males to females for mother, but not father, affected was 1.3 (SD = 1.4) and for father, but not mother, affected was 0.29 (SD = 1.0). A Mann–Whitney U test was used to assess whether there was significant difference between the number of male and female children born to affected mothers vs affected fathers. Results demonstrated a significant between group difference ($P < 0.02$). An example of a family tree for a paternally transmitted case and a maternally transmitted case is shown in Fig. 3.

DISCUSSION

Because of the high male:female sex-ratio known to occur among language-impaired children, and family aggregation for the disorder, [50] sex-influenced modes of genetic transmission were investigated. The pattern of family history data found in this study fails to provide support for sex-linkage hypotheses. Male and female language-impaired probands show equal propensity to have an affected mother or father. Furthermore, language-impaired boys and girls do not differ significantly in rate of affected siblings or sex of affected siblings. These findings agree with previous reports for a similar developmental communication disorder, dyslexia [6–8, 23, 35, 57]. On the other hand, highly consistent data, implicating familial factors underlying the high proportion of males to females affected with language disorder, were found in this study. There was a 2.5:1, male:female sex-ratio in the language-impaired population, identified by research criteria, who participated in this study. Interestingly, probands without an affected parent (and therefore putatively less genetic predisposition) failed to show the expected significant increase of boys to girls with language/learning disorders. However, probands with an affected parent had a significant 3:1, male:female sex-ratio. When the affected parent was the father, the sex-ratio was 1.8:1. However, when the affected parent was the mother, the sex-ratio was 4:1. This ratio increased to 5:1 for probands with both parents affected. These data demonstrate that the increased incidence of males to females with language/learning impairments, so well documented in the literature, occurred in this sample primarily in those language-impaired children with affected parents, and more so in those with affected mothers than affected fathers.

Unexpected sex-ratios were also found in the siblings of language-impaired probands. Because it is known that more boys than girls are affected with the disorder, it was not unususal to find that among the *affected* siblings there was a 2.5:1 sex-ratio. However, it was unexpected to find that in absolute numbers, there were twice as many males as females born

**SEX RATIO OF OFFSPRING BY
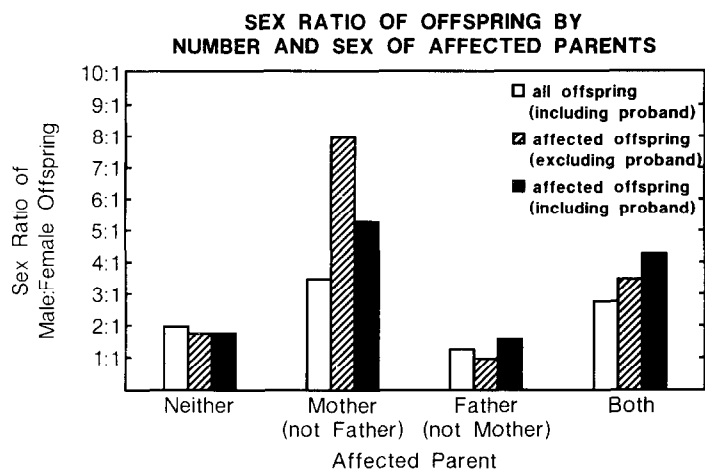NUMBER AND SEX OF AFFECTED PARENTS**

FIG. 2. Offspring sex-ratios are shown for families with neither parent affected, mother but not father affected, father but not mother affected, and both parents affected. Sex-ratios are given for all offspring combined, only affected offspring (excluding proband) and all affected offspring (including proband).
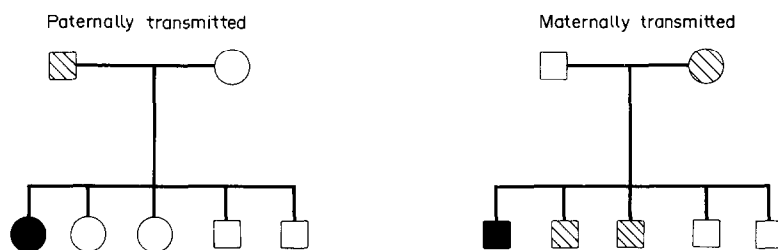

FIG. 3. Two family trees, one for a family of a language-impaired proband with a father but not mother affected, and one for a mother but not father affected are shown. Squares represent males and circles represent females. Probands are shown in black while affected parents and siblings are represented by cross-hatching. The propensity of male to female offspring in the family with an affected mother but not father is clearly demonstrated by these examples.

into the families of language-impaired children. Additional analyses again revealed that this unexpected sex-ratio in the siblings of language-impaired children occurred primarily in the families with only an affected mother (ratio 3:1) but not an affected father (ratio 1:1). This ratio increases dramatically when focusing only on affected children (not including probands) of affected parents. Affected mothers had eight times as many affected males as females. Affected fathers had equal numbers of affected males as females.

Reorganizing the above data by sex of affected parent, we find that affected fathers have essentially the expected 1:1 offspring sex-ratio, almost twice as many offspring non-affected as affected, and a 1:1 sex-ratio in absolute numbers of affected offspring (offspring-ratios do not include probands). On the other hand, affected mothers have a 3:1, male:female offspring-ratio, equal numbers of affected and non-affected offspring, and an approximate 5:1 sex-ratio in absolute numbers of affected offspring. This ratio rises to 8:1 when cases with only an affected mother are considered separately. It remains at 1:1 in cases where the father is the single affected parent. In other words, in this sample, for those families with affected

parents, male and female offspring were equally likely to be affected, but families with affected mothers had a disproportionate background frequency of male births, with these mothers being three times as likely to have male children. Half of these children were affected, giving rise to the observed predominance of boys with language disabilities. A similar pattern was found to account for the sex-ratio frequencies observed in the probands.

One of the most confusing issues that presently exists in the literature on the possible genetic basis of developmental dyslexia, a closely related, communicative learning disorder of childhood, concerns sex effects. Authors consistently report a 3–4:1, male:female ratio among probands; yet, when siblings are examined, it is reported that impairment rates are approximately equal, approaching 50% for both sexes [6–8, 23, 35, 37, 57]. SLADEN [46] addressed this conflict in the literature by re-examining data from HALGREN'S [17] now landmark study on sex-ratios in dyslexia. The main purpose of Sladen's paper was the use of Halgren's original data to support a hypothesis of autosomal dominant transmission of dyslexia. However, pertinent to the present study, Sladen notes, in re-examination of Halgren's data, that there is a puzzling item in the table, that dyslexic mothers had, altogether, 70 sons but only 34 daughters. Sladen suggests that this should be examined in future studies. These data provide confirmation, from a different data set, of our findings of an unexpectedly high male:female offspring sex-ratio in the affected mothers of language/learning-impaired children.

ROBINSON [40] also recently reported data consistent with these findings. He collected family data on children attending three different schools for language-impaired children in England. He reports evidence of family aggregation for language/learning impairment. He also lists the siblings of the language-impaired children as consisting of 136 brothers, but only 89 sisters.

Although the data from the present study fail to support a sex-linked mode of genetic transmission, the pattern of family aggregation data found, if genetically influenced, would be compatible with autosomal dominant transmission, with greater penetrance through mothers than through fathers. In autosomal dominant disorders, only one gene is necessary to express the disorder. If only one parent is carrying the gene, 50% of offspring will be affected; when both parents carry the gene, 75% of their offspring will be affected. Autosomal dominant disorders are also characterized by a high rate of spontaneous mutation and variable penetrance.

Among the language-impaired families in this study, there was an overall rate of 60% of offspring affected (including probands): 62% of male and 55% of female offspring were affected. Figure 4 shows the distribution of affected offspring, excluding probands. In families with only one parent affected, only 26% of the offspring of affected fathers were affected, whereas 53% of the offspring of affected mothers were affected. When both parents were affected, 50% of their offspring were affected, whereas when neither parent was affected, 33% of their offspring were affected.

Greater penetrance through mothers was found in this study. Both genetic and/or environmental factors might contribute to this finding. Autosomal dominant genetic disorders, with greater penetrance through the mother, have been reported. For example, myotonic dystrophy, a muscular disorder, is passed on differently by mothers than by fathers, with the neonatal, more severe form being transmitted primarily through the mother [10, 18]. It is also known that, although females are less prone to neurodevelopmental disorders, when such conditions do arise in females, a more severe form is usually manifest [53].
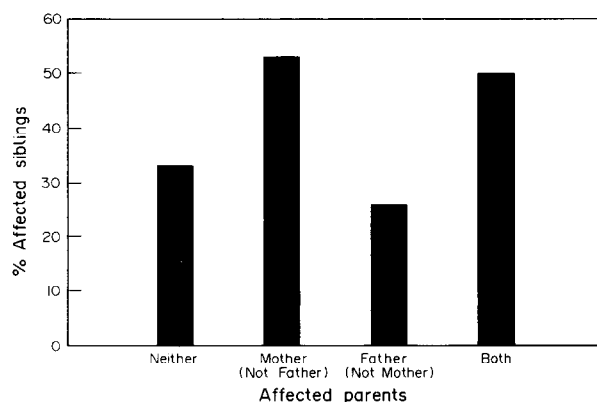
FIG. 4. The percent of affected siblings of language-impaired children are presented separately for families with neither parent affected, mother but not father affected, father but not mother affected, and both parents affected.

The increase of male to female offspring in families with language-impaired mothers could indicate an increased rate of spontaneous abortion early in pregnacy (increased fetal wastage), restricted to females. If this were the case, it would suggest that whatever trait was being transmitted would be more serious or potentially lethal in its female form, but compatible with survival (albeit afflicted) in its male form. On the other hand, greater phenotypic impairment in mothers may be passed to offspring environmentally, through mother–child interaction, which is known to play a role in language development [55]. Such environmental factors might interact with genetic factors to result in the disproportionately high incidence of affected offspring of affected mothers. SHAYWITZ et al. [44] suggest another potential environmental explanation for sex-ratio differences. They report that the increased incidence of boys with dyslexia may represent increased teacher referrals for special school services for boys, who more often are characterized by behavior as well as learning problems, than for girls. However, this may be less the case for severe developmental language disorders which can be precisely identified based on quantitative measures well before the child reaches school age.

Whereas environmental factors might contribute to the increased incidence of affected offspring of affected mothers, they cannot explain the dramatic and consistent pattern of absolute background male to female sex-ratio differences found in these families. For such explanations, factors affecting the secondary sex-ratio in humans must be evaluated. In studies investigating factors affecting the secondary sex-ratio in humans, increased male births have been most often associated with maternal stress and abnormal levels of gonadal hormones, especially testosterone [20]. Interestingly, both the effects of stress on hormonal secretion, and the effects of hormones on brain development have also been implicated in neurodevelopmental language and learning disorders [14, 15, 27]. GESCHWIND and BEHAN [14, 15] have suggested that developmental learning disorders may be linked to both left-handedness and immune disorders through the action of testosterone on brain development. These authors propose that abnormal testosterone levels, or unusual sensitivity to testosterone during fetal life, can alter brain anatomy such that normal cerebral asymmetry fails to develop. In support of this hypothesis, GALABURDA and KEMPER [12] reported finding neuronal migration abnormalities, as well as lack of expected cerebral asymmetry in

the temporal speech areas, from post-mortem morphological evaluations of the brains of dyslexic individuals. Consistent with these findings, JERNIGAN *et al.* [21] reported a significant increase in reversed asymmetry of post-sylvian cerebrum in developmental dysphasics, as compared to matched controls, from *in vivo* magnetic resonance imaging (MRI) studies. The degree of reversed asymmetry in post-sylvian regions was found to correlate highly ($r = 0.72$, $P < 0.02$) with decreased grey matter proportions and increased fluid proportions in this region. The finding that gonadal hormones also affect neuroanatomical cerebral lateralization in rats [9] and both neural lateralization and sex differences associated with vocal control in birds [33, 34] adds further support to a link between gonadal hormones, sex-ratio, and cerebral lateralization.

Another line of evidence possibly linking abberant testosterone levels to language/learning disabilities comes from studies of children with Kleinefelter's syndrome. Children with Kleinefelter's syndrome (47 XXY) have abnormal levels of testosterone. These boys also develop significant language/learning disorders that cannot be attributed to general mental retardation. In fact, they have been reported to show a strikingly similar neuropsychological profile to that reported for children with specific developmental language disorders [16]. Thus, there are several independent lines of research across species that have linked aberrant gonadal hormone levels to elevated male:female sex-ratios, abnormal brain development, and language/learning disorders.

In conclusion, the pattern of data reported here for families of language/learning-impaired children may reflect influences of genetic, hormonal, immunological or environmental factors; or an interaction between one or more of these factors. It must be noted, however, that the degree of ascertainment bias, introduced by identifying families for study through an affected member (proband), cannot be estimated for this study. Thus, it is possible that ascertainment bias may have also contributed to these data, with families with more than one affected member perhaps being more likely to volunteer for participation in research. However, it is unlikely that ascertainment bias alone could acccount for the highly significant sex-ratio differences observed in this study, particularly those observed in the unaffected siblings of probands, or the consistency in the familial pattern of these sex-ratio differences in both the probands and their siblings.

There have been very few familial studies of children with well-documented specific developmental language disorders. The significant and consistent findings of familial aggregation and aberrant sex-ratios reported in this study, based on self-report question-naire data, suggest that direct evaluations of first-degree relatives of language-impaired children are warranted, indeed necessary, to confirm these findings and better specify precise estimates for further genetic studies. Other studies designed to test, in detail, the communication skills of family members of children with specific developmental language impairment will be necessary to confirm and extend these findings based on self-report data. Hormonal studies of both affected and non-affected mothers of language/learning-impaired children also might be revealing in light of hypotheses linking testosterone to both increased male:female sex ratios and developmental communication disorders.

REFERENCES

1. ARAM, D. M. and NATION, J. E. *Child Language Disorders.* C. V. Mosby, St. Louis, 1982.
2. ARNOLD, G. E. The genetic background of developmental language disorders. *Folia Phoniatr.* 13, 246 254, 1961.

3. BEITCHMAN, J. H., NAIR, R., FERGUSON, M. and PATEL, P. G. Prevalence of psychiatric disorders in children with speech and language disorders. *J. Am. Acad. Child Psychiatry* **25**, 528–535, 1986.
4. BISHOP, D. V. M. and EDMUNDSON, A. Is otitis media a major cause of specific developmental language disorders? *Br. J. Disord. Commun.* **21**, 321–338, 1986.
5. BORGES-OSORIO, M. R. and SALZANO, F. M. Language disabilities in 3 twin pairs and their relatives. *Acta Genet. Med. Gemellol.* (Roma) **34**(1–2), 95–100, 1985.
6. CHILDS, B. and FINUCCI, J. M. The genetics of learning disabilities. In *Human Genetics: Possibilities and Realities*, R. PORTER and M. O'CONNER (Editors), pp. 359–376. Excerpta Medica, **66**, New York, 1979.
7. DECKER, S. N. and DEFRIES, J. C. Cognitive ability profiles in families of reading disabled children. *J. Learn. Disab.* **13**, 517–522, 1980.
8. DEFRIES, J. C., SINGER, S. M., FOCH, T. T. and LEWITTER, F. I. Familial nature of reading disability. *Br. J. Psychiatry* **132**, 361–367, 1978.
9. DIAMOND, M. C. Sex differences in the morphology of the rat forebrain. *Brain Res. Rev.* **12**, 235–240, 1987.
10. FRIED, K., PAJEWSKI, M., MUNDEL, G., CASPI, E. AND SPIRA, R. Thin ribs in neonatal myotonic dystrophy. *Clin. Genet.* **7**, 417–420, 1975.
11. FRIEDRICH, U., DALBY, M., STAEHELIN-JENSEN, T. and BRUUN-PETERSEN, G. Chromosomal studies of children with developmental language retardation. *Dev. Med. Child Neurol.* **24**, 645–652, 1982.
12. GALABURDA, A. M. and KEMPER, T. M. Cytoarcritectonic abnormalities in developmental dyslexia: a case study. *Ann. Neurol.* **6**, 94–100, 1979.
13. GARVEY, M. and MUTTON, D. E. Sex chromosome aberrations and speech development. *Archs Dis. Child.* **48**, 937–941, 1973.
14. GESCHWIND, N. and BEHAN, P. O. Left-handedness: association with immune disease, migraine and developmental learning disorders. *Proc. natn Acad. Sci. U.S.A.*, 5097–5100, 1982.
15. GESCHWIND, N. and BEHAN, P. O. Laterality, hormones and immunity. In *Neural Modulation of Immunity*, R. GUILLEMIN, M. COHN and T. MELNECHUK (Editors), pp. 73–80. Raven Press, New York, 1984.
16. GRAHAM, J. M., JR, BASHIR, A. S., STARK, R. E. and TALLAL, P. Auditory processing abilities in unselected XXY boys. *Clin. Res.* **30**, 118A, 1982.
17. HALGREN, B. Specific dyslexia: a clinical and genetic study. *Acta Psychiatr. Neurol.* **65**, 1–287, 1950.
18. HARPER, P. S. Congenital myotonic dystrophy in Britain: clinical aspects. *Archs Dis. Child.* **50**, 505–513, 1975.
19. INGRAM, T. T. S. Specific developmental disorders of speech in childhood. *Brain* **82**, 450–467, 1959.
20. JAMES, W. H. Hormonal control of sex ratio. *J. Theoret. Biol.* **118**, 427–441, 1986.
21. JERNIGAN, T. L., TALLAL, P. and HESSELINK, J. Cerebral morphology on magnetic resonance Tdevelopmental dysphasia. *Soc. Neurosci. Abstr.* **13**(1), 651, 1987.
22. KIDD, K. K. Genetic models of stuttering. *J. Fluenc. Discord.* **5**, 187–201.
23. LEWITTER, F. I., DEFRIES, J. C. and ELSTON, R. C. Genetic models of reading disability. *Behav. Genet.* **10**, 9–30, 1980.
24. LUDLOW, C. L. and COOPER, J. A. (Editors) *Genetic Aspects of Speech and Language Disorders*. Academic Press, New York, 1983.
25. MONEY, J. Turner's syndrome and parietal lobe functions. *Cortex* **9**, 358–393, 1973.
26. MUTTON, D. E. and LEA, J. Chromosome studies of children with specific speech and language delay. *Dev. Med. Child Neurol.* **22**, 588–594, 1980.
27. MCEWEN, B. S. Hormones and the brain. In *Childhood Learning Disabilities and Prenatal Risk*, C. C. BROWN and L. B. SILVER (Editors), pp. 11–16. Johnson & Johnson, 1983.
28. MCREADY, E. B. Defects in the zone of language (word-deafness and word-blindness) and their influence in education and behaviour. *Am. J. Psychiatry* **6**, 267, 1926.
29. NETLEY, C. Sex chromosome abnormalities and the development of verbal and non-verbal abilities. In *Genetic Aspects of Speech and Language Disorders*, C. L. LUDLOW and J. S. COOPER (Editors), pp. 179–195. Academic Press, New York, 1983.
30. NETLEY, C. and ROVET, J. Verbal deficits in children with 47, XXY and 47, XXX karyotypes: a descriptive and experimental study. *Brain Lang.* **17**, 58–72, 1982.
31. NIELSEN, J. and SILLESEN, I. Follow-up till age 2–4 of unselected children with sex-chromosome abnormalities. *Hum. Genet.* **33**, 241–257, 1976.
32. NIELSEN, J., SORENSON, A. M. and SORENSON, K. Mental development of unselected children with sex-chromosome abnormalities. *Hum. Genet.* **59**, 324–332, 1981.
33. NOTTEBOHM, F. Ontogeny of bird song. *Science* **167**, 950–956, 1970.
34. NOTTEBOHM, F. Neural lateralization of vocal control in a passerine bird. I. Song. *J. exp. Zool.* **177**, 229–262, 1971.
35. OMENN, G. S. and WEBER, B. A. Dyslexia: search for phenotypic and genetic heterogeneity. *Am. J. Med. Gen.* **1**, 333–342, 1978.
36. PENNINGTON, B., PUCK, M. and ROBINSON, A. Language and cognitive development on 47 XXX females followed since birth. *Behav. Genet.* **10**, 31–41, 1980.

37. PENNINGTON, B. F. and SMITH, S. D. Genetic influences on learning disabilities and speech and language disorders. *Child Dev.* **54,** 369–387, 1983.
38. PUCK, M., TENNES, K., FRANKENBURG, W., BRYANT, K. and ROBINSON, A. Early childhood development of four boys with 47 XXY karyotype. *Clin. Genet.* **7,** 8–20, 1975.
39. RATCLIFFE, S. G. Speech and learning disorders in children with sex-chromosome abnormalities. *Dev. Med. Child Neurol.* **24,** 80–84, 1982.
40. ROBINSON, R. J. The causes of language disorders. In *Proceedings of the 1st International Symposium on Specific Speech and Language Disorders in Children,* Reading, England. Association for all Speech Impaired Children. ISBN 0 9512499 0 8, Middlesex, England: HGA Printing Co., 1987.
41. ROBINSON, A., LUBS, H., NIELSEN, J. and SORENSEN, K. Summary of clinical findings: profiles of children with 47, XXY, 47, XXX and 47, XYY karyotypes. *Birth Defects* **15,** 261–266, 1979.
42. ROVET, J. and NETLEY, C. The mental rotation task performance of Turner syndrome subjects. *Behav. Genet.* **10,** 437–443, 1980.
43. SAMPLES, J. M. and LANE, V. W. Genetic possibilities in six siblings with specific language disorders. *Am. Sp.-Lang-Hear. Assoc.* **27**(12), 27–32, 1985.
44. SHAYWITZ, S. E., TOWLE, V. A., KESSNE, D. K. and SHAYWITZ, B. A. Prevalence of dyslexia in boys and girls in a epidemiological sample: contrasts between children identified by research criteria and by the school system. *Ann. Neurol.* **24,** 313–314, 1988.
45. SILVA, P. A. The prevalence, stability, and significance of developmental language delay in preschool children. *Dev. Med. Child Neurol.* **22,** 768–777, 1980.
46. SLADEN, B. K. Inheritance of dyslexia. *Bull. Orton Soc.* **20,** 30–40, 1970.
47. STEWART, D. *et al.* Growth and development of children with X and Y chromosome aneuploidy from infancy to pubertal age: The Toronto study. *Birth Defects* **18**(4), 1982.
48. TALLAL, P. and PIERCY, M. Developmental aphasia: rate of auditory processing and selective impairment of consonant perception. *Neuropsychologia* **12,** 83–93, 1974.
49. TALLAL, P. and PIERCY, M. Developmental aphasia: the perception of brief vowels and extended stop consonants. *Neuropsychologia* **13,** 69–74, 1975.
50. TALLAL, P., ROSS, R. and CURTISS, S. Familial aggregation in specific language impairment. *J. Speech Hear. Disord.* **54,** 1989.
51. TALLAL, P., STARK, R. and MELLITS, D. The developmental language disorder. *Neuropsychologia* **23,** 527–526, 1985.
52. TALLAL, P., STARK, R. and MELLITS, D. Identification of language impaired children on the basis of rapid perception and production skills. *Brain Lang.* **25,** 314–322, 1985.
53. TAYLOR, D. C., OUNSTED, C. The nature of gender differences explored through ontogenetic analysis of sex ratios in disease. In *Genetic Differences: Their Ontogeny and Significance,* C. OUNSTED, and D. C. TAYLOR (Editors). Churchill Livingstone, 1972.
54. TENNES, K. S., PUCK, M., BRYANT, K., FRANKENBURG, W. and ROBINSON, A. A developmental study of girls with trisomy X. *Am. J. Hum. Genet.* **27,** 71–80, 1975.
55. TIZARD, B., HUGHES, M., CARMICHAEL, H. and PINKERTON, G. Language and social class: is verbal deprivation a myth? *J. Child Psychol. Psychiat.* **24**(4), 533–542, 1983.
56. TUNCBILEK, E., KURULTAY, N. and BELGIN, E. Are sex-chromosome abnormalities a factor in speech delay? *Archs Dis. Child.* **53,** 831, 1978.
57. ZAHALKOVA, M., URZAL, V. and KLUBOUKOVA, E. Genetical investigation in dyslexia. *J. med. Gen.* **9,** 48–52, 1972.