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Cerebral configurations among the parents and siblings of language-disordered boys

Plante, Elena Margaret, Ph.D.

The University of Arizona, 1990
CEREBRAL CONFIGURATIONS AMONG THE PARENTS
AND SIBLINGS OF LANGUAGE-DISORDERED BOYS

by

Elena Margaret Plante

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A Dissertation Submitted to the Faculty of the
DEPARTMENT OF SPEECH AND HEARING SCIENCES
In Partial Fulfillment of the Requirements
For the Degree of
DOCTOR OF PHILOSOPHY
In the Graduate College
THE UNIVERSITY OF ARIZONA

1990
As members of the Final Examination Committee, we certify that we have read the dissertation prepared by Elena Margaret Plante entitled Cerebral configurations among the parents and siblings of language-disordered boys and recommend that it be accepted as fulfilling the dissertation requirement for the Degree of Doctor of Philosophy.

Theodore T. Giammarco  
Judith L. Grant

Final approval and acceptance of this dissertation is contingent upon the candidate's submission of the final copy of the dissertation to the Graduate College.

I hereby certify that I have read this dissertation prepared under my direction and recommend that it be accepted as fulfilling the dissertation requirement.

Dissertation Director

Date
STATEMENT BY AUTHOR

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Signed Elena Plante
Acknowledgements

I thank each of my doctoral committee members, Drs. Anna Binkiewicz, Judith Lauter, Theodore Glattke, and Steven Rapcsak for providing advice and professional opportunities. Dr. Joachim Seeger and Mrs. Rebecca Vance were instrumental in providing the support and resources necessary to establish the line of research that led to this dissertation. I thank Dr. Linda Swisher who created a setting in which I was challenged to learn and who provided the resources, guidance, and opportunities to do so.
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Four families that include a specifically language-impaired (SLI) boy were studied to test the hypothesis that developmental language disorders are biologically transmittable and to further describe the neuroanatomical correlates of the disorder. A majority of the parents and siblings of the SLI boys also experienced communication difficulty (i.e., difficulty with speech, language, or academic skills). Evidence of communication difficulty was paired on an individual basis with neuroanatomical data obtained through quantitative analysis of magnetic resonance imaging (MRI) scans. Atypical perisylvian asymmetries were documented in a majority of the parents ($p < .05$) and were closely associated ($p = .84$) with a history of communication difficulty. These findings provide evidence that the disorder is biologically transmittable. In addition, language-disordered siblings of SLI boys also had atypical perisylvian asymmetries. This finding suggests that atypical perisylvian asymmetries reflect biological factors that place some families at risk for language impairment.

Measures of seven additional cerebral regions established that areas outside the perisylvian are often atypical in size. These measures demonstrate that
neuroanatomical effects were bilateral and widespread. Thus, the neuroanatomical profile for developmental language disorder differs from the profile typically associated with cases of acquired language disorder, which typically result from damage to the left perisylvian area in a premorbidly normal brain. In contrast, neuroanatomical correlates of developmental language disorder reflect a probable disturbance of prenatal brain development.
Neuroanatomical background

Neuroanatomical studies provide information into the biological foundations of developmental language disorders. Two types of neuroanatomical studies are available: autopsy and imaging. Autopsy studies offer the best opportunity for detailed study of both gross anatomy and the underlying cellular architectonics. However, with autopsy studies, the behavioral features of a disorder are necessarily described retrospectively. Thus, adequate documentation of behavior is often unavailable. In contrast, noninvasive in-vivo imaging studies afford the opportunity to study the cerebral anatomy of subjects whose behavioral strengths and deficits can be documented. This advantage is offset by the relatively poor resolution of imaging studies. Current imaging capabilities are only capable of detecting lesions or developmental abnormalities that are sufficiently widespread that they alter gross anatomy. Therefore, while imaging studies can be used to document an apparent departure from the typical size or configuration of an anatomical region, autopsy examination is necessary to
determine whether changes in the cellular architecture has produced the effect.

Neuroanatomical studies have established a strong relation between certain acquired language disorders in adults and lesions of the left perisylvian cortex (see Rubens, 1984 for a review). Preliminary evidence from neuroanatomical studies of subjects with a developmental disorder involving impaired language suggests a brain-language relation. Alterations in both the cellular and gross anatomy have been noted. Landau, Goldstein, and Kleffner (1960) documented a bilateral gross degeneration of the insulae and operculae along with polymicrogyri in the posterior sylvian region in a multiply handicapped boy whose major behavioral deficit was a severe language disorder. Subcortical degeneration of the cerebral peduncles and geniculate nuclei were also noted in this child.

Alterations of both cellular and gross anatomy were also noted in a study of four males with developmental dyslexia (Galaburda, Sherman, Rosen, Aboiwtz, & Geschwind, 1985). In at least three of the four subjects, the dyslexia was associated with speech or language difficulties. Autopsy revealed cortical ectopias, which were most numerous in the left perisylvian area in all four subjects. One subject also had polymicrogyri in the posterior sylvian
region. The plana temporale, which typically is larger in the left than in the right hemisphere (Chi, Dooling, & Gilles, 1977a; Geschwind & Levitsky, 1968; Wada, Clarke, & Hamm, 1975; Witelson & Pallie, 1973), was symmetrical in all four subjects.

Perisylvian symmetry has also been documented in an autopsy study of a girl who had a severe expressive language disorder along with attention deficit disorder (Cohen, Campbell, & Yaghmai, 1988). The atypical symmetry was accompanied by a single dysplastic region in the left frontal opercular region. A comparable finding occurred in an magnetic resonance imaging (MRI) study of four boys with specific language impairment (SLI), each of whom had an expressive impairment involving grammatical morphemes (Plante, Swisher, Vance, & Rapscak, 1990). The perisylvian areas of two of the boys were symmetrical, whereas a reversed (right > left) asymmetry was noted for a third.

In summary, both autopsy and imaging studies draw attention to a variety of perisylvian findings. Frank abnormalities at the cellular level occurred bilaterally in some subjects (Galaburda et al, 1985; Landau et al, 1960) and unilaterally in one (Cohen et al, 1988). When atypical asymmetries were documented, these resulted from a variety of left-right perisylvian configurations. In the subjects
described as having dyslexia, symmetry resulted because the
left planum temporale was of the expected size, while the
right planum was atypically large (Galaburda et al., 1985).
A similar finding was also noted for one SLI boy (Plante,
Swisher, & Vance, 1989). In this child, the right
perisylvian area was larger than average while the left was
of the expected size. Additional SLI boys with atypical
perisylvian asymmetries had different perisylvian
configurations. One boy had a right perisylvian area that
was average size whereas the left was smaller than expected.
Another had left and right perisylvian areas that were both
smaller than average (Plante et al., 1990).

The nature of these neuroanatomical findings indicates
the abnormalities occurred during the course of prenatal
brain development (Galaburda et al., 1985; Plante et al.,
1989). For example, polymicrogyri can be experimentally
induced by lesioning the mammalian brain during the period
of cell migration. The extent of gyral abnormality is
related to the time of lesion, with the more extensive
abnormalities resulting from an early time of lesion (Dvorak
ectopias are also thought to occur during the period of cell
migration as the result of misplaced migratory neurons
(Caviness, Evrard, & Lyon, 1978; Sherman, Galaburda, &
Geschwind, 1983). The presence of atypical cerebral asymmetries also suggests a prenatal effect. The normal left > right pattern of perisylvian asymmetries first appears during the third trimester (Chi et al, 1977a). After this time, the left > right pattern of plana asymmetry predominates in infants and children (Chi et al, 1977a; Wada, et al 1975; Witelson & Pallie, 1973) and adults (Geschwind & Levitsky, 1968; Wada et al, 1975; Witelson & Pallie, 1973).

Several autopsy studies have addressed the issue of possible gender differences in the pattern of asymmetry. Most studies have not found gender differences for size of the right and left plana temporale or the degree of asymmetry of cerebral structures (Chi et al, 1977a, Koff, Naeser, Pieniadz, Foundas, & Levine, 1986; McShane, Risse, & Rubens, 1984; Wada et al, 1975). Two studies (Bear, Schiff, Saver, Greenberg, & Freeman, 1986; Wada et al, 1975) report that subgroups of subjects who have an atypical, right > left asymmetry tend to have more female than male members.

Atypical asymmetries have been documented for regions that extend beyond the perisylvian areas. Rosenberger and Hier (1980) used computerized tomography (CT) in a study of learning-disabled subjects. These subjects all had verbal intelligence test scores that were lower than their
performance scores. Some subjects also had a history of "delayed speech." Approximately one half of the subjects with a history of "delayed speech" also had a reversed (right > left) asymmetry of the occipital poles. A third of the remaining learning-disabled subjects also had a reversed asymmetry pattern.

Using magnetic resonance imaging (MRI), Jernigan et al (1987) studied specifically language-impaired (SLI) children. In approximately half of the children, an atypical pattern of asymmetry (right > left) was noted for a cerebral region bounded by the sylvian fissure anteriorly and the occipital poles posteriorly. Plante et al (1990) documented atypical asymmetries (left > right) of the cerebral hemispheres in three of four SLI boys. These studies suggest that the developmental effects producing atypical neuroanatomical patterns in language-disordered children may be relatively widespread. The anatomical areas that contribute to this atypical hemispheric asymmetry have not yet been identified.

A description of the relative effects on neuroanatomy would provide further insight into the mechanism(s) that produced the atypical neuroanatomical patterns. Studies of language-disordered children reveal neuroanatomical variability across subjects. Such inter-subject variability
may reflect etiological differences. Alternatively, anatomical variation may be related to interactions between the causal agent and the stage of brain maturation in any given subject (Plante et al., 1989). The gyral configurations of the perisylvian area mature relatively late (Chi, Dooling, & Gilles, 1977b). A finding that late-developing structures are most often atypical in size would suggest the time of greatest neuroanatomical effect occurs during late gestation. If the probability that a structure will be atypical increases in parallel with the general maturational gradient for gyri, intersubject heterogeneity might actually reflect differences in the onset and severity of the causal agent(s). Thus, differences in neuroanatomical effect would represent a range of one biological effect that occurs at different times during development.

Evidence for transmission of language disorders

The atypical neuroanatomical findings in language-disordered individuals may be the result of an agent that is transmitted through families. If this is true, the parents and siblings of language-disordered children should show the neuroanatomical effect as well. Although such a
transmittable neuroanatomical effect has yet to be demonstrated in the families of language-disordered children, there is behavioral evidence that the disorder runs through families. Early evidence of familial tendencies toward developmental language disorders came from reports of selected families that include multiple cases of a speech or language disorder (Arnold, 1961; Samples & Lane, 1985).

This familial tendency has been substantiated by studies examining groups of language-disordered children and their families. Several studies have relied on questionnaires completed by a parent of language-disordered and control children, detailing the language and academic histories of all family members (Bishop & Edmundson, 1986; Neils & Aram, 1986; Tallal, Ross, & Curtiss, 1989a & b; Tomblin, 1989). These studies report that if a child is language disordered, more language or learning problems are reported for first-degree relatives than if a child is not language-disordered. Tomblin (1989), reported that 51% of the impaired probands had at least one language-impaired relative. A relative was considered language disordered only if he or she had received speech or language therapy. Tallal et al (1989a & b), using a criterion of self-report of language disorder, reading difficulties, or academic
failure to indicate signs of impairment found that 77% of SLI probands had at least one impaired relative. Fathers reported some form of impairment more often than mothers (Neils & Aram, 1986; Tallal, et al, 1989a; Tomblin, 1989). However, there is some evidence to suggest that impaired mothers have more language-disordered children than do impaired fathers or control parents (Tallal et al, 1989a). Across studies, language-disordered probands have more impaired brothers than sisters (Neils & Aram, 1986; Tallal, et al, 1989a; Tomblin, 1989). This may be confounded by a skewed sex ratio favoring boys in families of language-impaired children (Tallal et al, 1989b).

The questionnaire method may include a reporting bias favoring families that already include a language-disordered child. These families are likely to be more sensitive to the signs of disordered language than other families. It is possible that the results of the familial studies reflect inflated estimates in the families of language-disordered children, and underestimates the prevalence of language disorder in the families of controls. Standardized testing provides a more objective method of assessing the prevalence of disordered language than does self report. Standardized testing was used to determine differences in language skills for normal and reading-impaired children and their families
(DeFries, Singer, Foch, & Lewitter, 1978). Reading-impaired children, as a group, performed poorly relative to controls on measures of language. Parents and siblings of reading-impaired children obtained lower test scores for reading, spelling, and language-based measures than did controls. Language skills showing significant differences between groups included grammatical closure, auditory memory, and verbal analogies. Thus, a familial tendency towards poor language skills has been documented using objective as well as subjective methods.

In any group of language-disordered children, not all will have a family history for the disorder. Byrne, Willerman, and Ashmore (1974) adapted a model originally used to describe distributions of mentally retarded children and suggested that there may be two groups of language-disordered children which can be identified by factors such as severity and family history. They found that children with moderately impaired language skills generally had a lower socioeconomic level and more language-disordered relatives than children with severely impaired language skills. They suggest that the moderately impaired children were more likely to represent the extremes of the normal distribution for language skills. Furthermore, they suggested the children with severe language impairment may
represent a biologically different population, in which the disorder is more likely to be secondary to acquired lesions or trauma.

The findings of this study should be interpreted with caution. The measure used to document language impairment in these children was the Illinois Test of Psycholinguistic Abilities (Kirk, McCarthy & Kirk, 1968). Of this battery's eight subtests, only two appear to reflect skills that are weak in language impaired children (Fundudis, Kolvin, & Garside, 1979). The remaining six subtests probably reflect general cognition. Therefore, the authors may have inadvertently been testing distributions of children with moderate and severe cognitive skill deficits rather than language skill deficits. A later study that hypothesized an association between the severity of a language disorder and family history failed to confirm such a relationship (Neils & Aram, 1986).

Implications of a transmittable effect

Factors such as trauma or stroke are unlikely explanations for multiple cases of impairment within a family. A family tendency towards language or learning disorders suggests a genetic contribution to the disorder although the available data does not clearly conform to
classic models of genetic transmission (Neils & Aram, 1986; Tallal et al, 1989a; Tomblin, 1989). Tomblin (1989) points out that rearing practices that restrict language development cannot be ruled out when multiple family members have poor language skills. However, rearing practices would not explain the atypical neuroanatomical findings in SLI children. An environmental factor, such as a toxin, can affect multiple family members. To date, there is no evidence to implicate any toxin as a common cause of developmental language disorders. Both parents and children would have to be exposed to the same toxic effects in utero to explain similar neuroanatomical findings across generations.

A fourth explanation proposes hormonal effects on development (Geschwind & Behan, 1982; Plante et al, 1989; Tallal et al, 1989b). A hormonal explanation is consistent with the constellation of behavioral and biological characteristics associated with developmental language disorders. A hormonal effect could explain transmission through families (cf. Perakis & Stylianopoulou, 1986) as well as the atypical sex ratio in families of language-impaired children (Tallal et al, 1989b). Subjects with developmental disorders involving gonadal hormones tend to have poor language skills and learning difficulties
(McCardle & Wilson, 1987; Perlman, 1973). Gonadal hormones are known to influence brain development in animals, and may explain the anatomical effects seen in language-impaired subjects (Galaburda et al., 1985; Plante et al., 1990).

If a transmittable factor produces language impairment and also alters brain development, the relatives of language-impaired probands should also have a high rate of atypical cerebral configurations. Preliminary evidence supports this hypothesis. Atypical brain configurations have been noted in the normally developing twin sister of a language-impaired boy (Plante et al., 1989). Atypical perisylvian asymmetries were also found in a male who reported having a brother who had received language therapy. This individual was one of a group of males who had agreed to have an MRI scan as part of a research program (Plante, unpublished data). A more systematic study of the siblings of language-disordered children is needed to verify these preliminary findings. Atypical neuroanatomical findings in parents of language-disordered children would strengthen the argument that a transmittable effect contributes to developmental language disorders.

The consistency of neuroanatomical configurations across subjects is also potentially important. A consistent pattern of findings across subjects who share the same
behavioral diagnosis would suggest a single effect is operating on the developing brain. In a previous study (Plante et al, 1990), atypical cerebral asymmetries were found across subjects, with some degree of individual variability noted. This variability may represent a range of one biological effect, or separate effects operating across subjects. When subjects consist of first-degree relatives (parents and their children), their biological backgrounds can be considered highly similar. Should such subjects show atypical cerebral configurations, inter-subject heterogeneity is more likely to reflect a range produced by one biological effect rather than separate effects across family members.

**Statement of Purpose and Significance**

This study will describe the neuroanatomical profiles in families containing a specifically language-impaired boy, in order to assess the type and frequency of atypical anatomical profiles. The presence of atypical cerebral configurations in parents of specifically language-impaired boys would support the theory that this type of language impairment is the result of a biological factor that is transmitted through families. The neuroanatomical profiles among first-degree relatives will help to establish a range that is likely to reflect a single biological agent. The
identification of neuroanatomical regions that are frequently atypical will provide insight into the nature of the presumed biological agent.

Research Questions

The study is designed to answer the following research questions:

1. Do atypical perisylvian asymmetries occur in parents of SLI boys?
2. To what extent are atypical perisylvian asymmetries associated with evidence suggesting a language disorder in the parents of SLI boys?
3. What is the range of cerebral effect as seen among first-degree relatives?
4. What neuroanatomical regions, in addition to the perisylvian areas, are atypical in individuals with a personal or family history of language impairment.
Subjects

Members of four families that include at least one boy with SLI (the proband) participated in this study. A brief description of each family follows.

Family 1:

A 46-year-old father and 39-year-old mother, along with three male children (ages 12;10, 7;0, and 5;4) are the members of Family 1. All family members consider themselves to be right handed, although the parents report left handedness among their blood relatives. All three sons were diagnosed as language impaired and were enrolled in therapy programs at the time of study. The mother reported the oldest son was born two months prematurely and spent his first month in an intensive care unit. He was identified as language impaired when he entered first grade. He has a history of poor articulation skills and difficulty with expressive language. At the time of study, he was experiencing difficulty with reading and writing as well as with expressive language skills. He was taking Ritalin at the time of study to manage hyperactivity. The second son's birth was described as unremarkable but he required surgery
to correct an imperforate anus. He has undergone additional surgery on the scrotum and testicles and has had tests to evaluate bladder control. He was enrolled in therapy for impaired language and poor articulation at age three years. These skills were still impaired at the time of study. The youngest son, the proband, was delivered three weeks prematurely and required oxygen after birth. He was enrolled in language therapy at age three years. His articulation skills were age appropriate. His expressive language skills were significantly below the level expected of a child his age.

Both parents report that they had language/learning problems as children similar to what they have observed in their sons. The father repeated first grade and entered the military service after grade nine. He later received a high school diploma and was employed as a materials handler at the time of study. The mother, a housewife, has a high school diploma and completed two years of post-secondary education. The father has four additional sons from two previous marriages. Two of these sons have developmental disabilities. Both parents have nephews who have been diagnosed as learning disabled. Both parents report twins (fraternal and identical) among their blood relatives.
Family 2:

Family 2 includes a 37-year-old father and a 31-year-old mother along with their two sons (ages 6;10 and 5;0) and a daughter (age 2;0). The father is left handed; all other family members are right handed. The mother reported each of her pregnancies were unremarkable. The first-born son appeared to be developing normally at the time of study. The daughter was too young to participate in this study, but also appeared to be developing language normally. The second-born son, the proband, was diagnosed as SLI and was enrolled in a therapy program at the time of this study. He was being treated for a severe articulation disorder and impaired language. His family first became concerned about his speech and language development when he was approximately two years of age.

Neither parent reported childhood difficulties with language or academic skills. The father completed a college degree and was employed as an engineer. He reported that he had "stuttered" until age five years. He also reported his sister had stuttered as well. The mother completed a college degree and was a housewife at the time of study. No developmental disorders were reported among the mother's relatives. The mother reported fraternal twins among her relatives.
Family 3:

The third family includes a father (age 57), a mother (age 39), two daughters (ages 11:5 and 8:6), and one son (age 9:6) who served as the proband for this family. The mother reported her pregnancies were unremarkable. General health of all children is reported to be unremarkable. The oldest daughter appeared to be developing normally. The proband has a history of speech and language impairment. His mother first noticed a problem with language development when he was approximately age two years. He started receiving therapy for poor articulation and impaired language at age three and was enrolled in a school serving "dyslexic" students at the time of study. The youngest daughter was receiving tutoring for reading in school and was being evaluated for language impairment at the time of study. She declined participation in this study because of apprehension about being inside the MRI scanner.

The father reported he had difficulties with speech and language development similar to those he observes in his son. The father reported his own speech was hard to understand until age six and he subsequently had difficulty learning to read in school. He reported that he does not enjoy reading. He completed nine years of schooling and was employed as a bus driver. He has a brother who also had
difficulty with speech and language development and has twin sons from an earlier marriage. The mother completed nine years of school and managed a small business at the time of study. She was born prematurely by approximately 6 weeks. She reported that she had a "lisp" as a young child. She reported no problems with language or academic skills.

Family 4:

The fourth family includes a father (age 46), mother (age 42), a son (the proband, age 8;2) and daughter (age 6;2). All family members consider themselves to be right handed. The mother reported that pregnancy and birth for each child was unremarkable. Both children had a history of middle-ear infections, but general health has otherwise been unremarkable. The proband has a history of delayed speech onset (first words appeared at approximately 19 months) and was diagnosed as SLI. He was enrolled in a school serving "dyslexic" children at the time of study. According to standardized testing, the daughter had significantly delayed articulation skills for her age. Although she performed well on most language tests, she was verbally reticent. An analysis of spontaneous language revealed mildly impaired expressive language skills and word-finding problems. She was not receiving speech or language services at the time of study. The parents had experienced one miscarriage prior to
the birth of their first child.

The mother considered herself dyslexic and reported she had used "baby talk" as late as kindergarten. She recalled having some difficulty learning in grade school and reported that reading takes her a "long time" and is "tiring." She also reported that she had a unilateral hearing loss as a child and attended a school for deaf and blind children for first grade. She reported that she "out grew" the hearing loss. She passed a pure-tone screening test at the time of study. The mother has a high school diploma and completed a year of post-secondary education. She was a housewife at the time of study. The father reported he had difficulty learning to read and reports he does not enjoy reading. He holds a masters degree and was teaching at the college level at the time of study. The father reported that his brother had difficulty with speech and language and considers him to be dyslexic. The mother has a nephew who is receiving educational services for dyslexia.

Subject recruitment and selection

Subjects were recruited by soliciting referrals of boys with SLI from agencies and professionals serving such children in the Tucson area. The term SLI was defined to the referral sources as a language impairment in the absence of deficits in cognitive, sensory, motor, and social-
emotional functioning.

After referral to the study, a diagnosis of SLI was confirmed through standardized testing and clinical judgement. A battery of standardized, norm-referenced tests was administered to each proband. The results of standardized testing are reported in Table 1. The test battery is described in Appendix A. The standardized tests chosen were those that reflected the skill areas of typical strengths (nonverbal, semantics) and weakness (morphosyntactic, speech articulation) that characterize SLI in children. The manuals provided sufficient information so that a z-score could be calculated. They were relatively strong psychometrically compared with other available instruments (McCaulley & Swisher, 1984), or had proven utility in identifying language-impaired children. All tests were administered by a certified speech-language pathologist or a graduate student under the supervision of a speech-language pathologist. Test score reliability was calculated on a point-to-point basis for all scorable test items. Median point-to-point reliability was 97 percent with a range between 75 and 100 percent agreement.

For children 7;11 years and younger, a spontaneous language sample was obtained for analysis. A twenty-minute play session with the child and an examiner was used to
Table 1.
Test profiles for probands and siblings.

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<td>sib 2</td>
<td>proband</td>
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<tr>
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<td>7;0</td>
<td>5;4</td>
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Tests:

**Nonverbal:**

K-ABC

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<td>sib 2</td>
<td>proband</td>
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**Vineland:**

Daily living

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<td>Socialization</td>
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<td>0.66</td>
<td>0.07</td>
<td>1.07</td>
</tr>
<tr>
<td>Motor</td>
<td>-1.33</td>
<td>-0.80</td>
<td>0.33</td>
<td>0.04</td>
</tr>
</tbody>
</table>

**Morpho-syntactic:**

TACL-R

<table>
<thead>
<tr>
<th></th>
<th>Family 1</th>
<th>Family 2</th>
<th>Family 3</th>
<th>Family 4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>sib 1</td>
<td>sib 2</td>
<td>proband</td>
<td>sib 1</td>
</tr>
<tr>
<td>Word classes</td>
<td>*</td>
<td>-0.25</td>
<td>-1.28</td>
<td>0.39</td>
</tr>
<tr>
<td>Grammatical</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morphemes</td>
<td>*</td>
<td>-0.71</td>
<td>0.74</td>
<td>-0.50</td>
</tr>
<tr>
<td>Elaborated</td>
<td>*</td>
<td>-0.20</td>
<td>0.02</td>
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</tr>
<tr>
<td>Sentences</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TOTKEN</td>
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<td>-0.60</td>
<td>NC</td>
<td>-0.26</td>
</tr>
<tr>
<td>ITPA</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Grammatical</td>
<td>*</td>
<td>-0.83</td>
<td>-0.67</td>
<td>-0.38</td>
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</table>

Table continues
<table>
<thead>
<tr>
<th>Family 1</th>
<th>Family 2</th>
<th>Family 3</th>
<th>Family 4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>gender:</strong></td>
<td>sib 1</td>
<td>sib 2</td>
<td>proband</td>
</tr>
<tr>
<td>Male</td>
<td>Male</td>
<td>Male</td>
<td>Male</td>
</tr>
<tr>
<td><strong>age:</strong></td>
<td>12:10</td>
<td>7:0</td>
<td>5:4</td>
</tr>
<tr>
<td>NSST-E</td>
<td>*</td>
<td>-6.46</td>
<td>-2.78</td>
</tr>
<tr>
<td>CELF-R Oral Direct.</td>
<td>-0.66</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Form. Sent.</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Recall. Sent.</td>
<td>-2.33</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Sent. Assembly</td>
<td>-1.33</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td><strong>Semantics:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PPVT-R</td>
<td>-0.33</td>
<td>0.22</td>
<td>0.00</td>
</tr>
<tr>
<td>OWEPVT</td>
<td>*</td>
<td>0.27</td>
<td>-0.47</td>
</tr>
<tr>
<td>CELF-R Word Classes</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Semantic Rel.</td>
<td>-1.00</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td><strong>Articulation:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Templin-Darley</td>
<td>*</td>
<td>0.48</td>
<td>-1.07</td>
</tr>
<tr>
<td><strong>Spontaneous language:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DSS</td>
<td>*</td>
<td>*</td>
<td>-1.00</td>
</tr>
</tbody>
</table>

* indicates that test was not given because it is not appropriate for the child's age.
NC indicates the test was discontinued because of unreliable responses.
gather the language sample. Children were given a choice of activities and toys to play with during this time. The play session was video taped and a corpus of the child's spontaneous language was transcribed from video tape. Four minutes of each child's language sample was selected at random to assess transcription reliability. Point-to-point reliability for transcribed words ranged between 98 and 99 percent for the samples obtained. A corpus of sentences were analyzed using Developmental Sentence Scoring (DSS) (Lee, 1974). For all but one child (sibling 1 in Family 4), the sentences included in the analysis were 50 consecutively occurring sentences that were spoken after the first five minutes of the play session had elapsed. The remaining child had so few sentences that utterances from the first five minutes had to be included to obtain a sample of 47 sentences. Point-to-point reliability for scorables items on the DSS ranged between 71 and 96 percent. Disagreements in scoring were resolved through joint review of the items in question.

To be selected for study, a proband had to demonstrate a significant impairment (lower 5 percent of the normative sample) in the comprehension or use of the morpho-syntactic components of language in the presence of normal nonverbal skills (upper 93 percent of the normative sample).
Table 2.  
Family history characteristics as reported by the parents of language-disordered boys.

<table>
<thead>
<tr>
<th></th>
<th>Family 1</th>
<th>Family 2</th>
<th>Family 3</th>
<th>Family 4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>maternal</td>
<td>paternal</td>
<td>maternal</td>
<td>paternal</td>
</tr>
<tr>
<td>Parental history:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Academic failure</td>
<td>no</td>
<td>grade 1</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>Reading difficulty</td>
<td>yes</td>
<td>yes</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>Speech or language difficulties</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>&quot;stuttered&quot;</td>
</tr>
<tr>
<td>Schooling completed</td>
<td>highschool + 2 yrs</td>
<td>grade 9</td>
<td>college</td>
<td>college</td>
</tr>
<tr>
<td>Handedness</td>
<td>right</td>
<td>right</td>
<td>right</td>
<td>left</td>
</tr>
<tr>
<td>Place of birth</td>
<td>New Ulm MN</td>
<td>Toledo OH</td>
<td>Salt Lake City UT</td>
<td>Columbus OH</td>
</tr>
<tr>
<td>Birth order</td>
<td>3rd</td>
<td>3rd</td>
<td>3rd</td>
<td>2nd</td>
</tr>
<tr>
<td>Mother's age at Subject's birth</td>
<td>26</td>
<td>31</td>
<td>31</td>
<td>16</td>
</tr>
<tr>
<td>Maternal miscarriages/stillbirths</td>
<td>2</td>
<td>none</td>
<td>none</td>
<td>none</td>
</tr>
</tbody>
</table>

Table continues
<table>
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<tr>
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<th>Family 1</th>
<th>Family 2</th>
<th>Family 3</th>
<th>Family 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;drug for miscarriage&quot;</td>
<td>father</td>
<td>father</td>
<td>father</td>
<td>father</td>
</tr>
<tr>
<td>&quot;father smoked&quot;</td>
<td>maternal</td>
<td>stress</td>
<td>smoked</td>
<td>smoked</td>
</tr>
<tr>
<td>fathers smoked</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risk factors at birth</td>
<td>caesarian</td>
<td>none</td>
<td>none</td>
<td>premature(6 weeks)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>breach forceps</td>
</tr>
<tr>
<td>Risk factors postnatally</td>
<td>none</td>
<td>none</td>
<td>none</td>
<td>none</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>otitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>none</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>none</td>
</tr>
<tr>
<td>Family history:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left handedness</td>
<td>yes</td>
<td>no</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>yes</td>
</tr>
<tr>
<td>Developmental disability</td>
<td>speech/</td>
<td>speech/</td>
<td>none</td>
<td>speech/</td>
</tr>
<tr>
<td></td>
<td>language</td>
<td>language</td>
<td>stuttering</td>
<td>dyslexia</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>none</td>
<td>dyslexia</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>language</td>
</tr>
<tr>
<td>Twinning</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>no</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>no</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>no</td>
</tr>
</tbody>
</table>
addition, to be selected for study, each proband had to pass a hearing screening at the time of testing. A passing performance consisted of reliable responses to 20 dB HL pure tones for at least three of the following frequencies: 500, 1000, 2000, and 4000 Hz. No selection criteria were set for performance on tests of vocabulary or articulation, or for the language sample analysis.

Two speech-language pathologists not otherwise connected with this study were asked to review compiled records for each potential proband. Records included past evaluations and therapy reports; tests of morpho-syntactic skills administered as part of this study were excluded. Each proband was judged language impaired by both speech-language pathologists.

When a potential proband was identified, the family was then invited to participate in this study. Families selected met three additional characteristics: children were monolingual English-speakers, both biological parents were willing to participate, and family members had no known neurological or developmental conditions that are known to alter brain morphology from normal (e.g. stroke, trauma, seizures). Nineteen potential probands were referred to the study. Four were rejected because their language skills were not significantly impaired. Three had other
Table 3.
Characteristics of comparison group.

Personal background:

Gender 11 males, 6 females
Ages: 20 to 47; median = 29
Handedness: right handed in all cases

Birth history:

Mother's age at birth: 20 - 38 years; median = 24
Birth order: 1 - 6; median = 2
Maternal miscarriages: 3 for male subjects
1 for female subjects
Pregnancy risk factors:
father smoked in 3 case for females
mother smoked in 1 case for females
males were not asked about parental smoking
Birth risk factors: 1 male was premature by 8 weeks

Family history:

Left handedness: 2 males
1 female
Developmental disorders: none reported
(this was a selection criterion)
Twinning: none reported
(this was a selection criterion)

Education:

years of education: 14-21 years (college)
median = 16 years (bachelor's degree)
special school services:
1 male (gifted & talented program)
1 female (articulation therapy for "r" only)
grade school failure: none reported
reading difficulty: none reported
handicapping conditions (e.g. attention deficit, hearing loss) in addition to impaired language. Two had a history of seizures and one was excluded because his mother had a history of seizures. Two qualified as SLI but were excluded from the study because the proband or a parent was unable to complete the MRI scan due to claustrophobic reactions. Three did not have both biological parents available for study. The subjects of the present study are the first four consecutive families that were not excluded on the bases described above.

When a family was selected, a case history was taken for each family member. Case histories covered medical, birth, developmental, educational, and family background in addition to speech and language history (see Appendix B). Information concerning the personal and family history for the mothers and the fathers in each family are reported in Table 2.

**Behavioral documentation for siblings**

The battery of standardized tests described in Appendix A was used to describe verbal and nonverbal skills in the siblings of each proband. The results of standardized testing for these subjects are provided in Table 1.
Procedures

Subjects were scanned in the axial plane through the full volume of the cerebral cortex. The slice angle was standardized for each subject by aligning the slice angle parallel to the frontal and occipital poles from a sagittal prescan view. Scans were gathered on a Toshiba 0.5 Tesla magnet. A spin-echo scan sequence (TR 2800, TE 90) was used that produces good distinctions between grey and white matter.

Scans from the subjects were compared with a group of comparison scans from volunteers who were without a history of language impairment. These scans (11 from males, 6 from females) were selected from a data bank (Plante, unpublished data) of volunteers for whom case history information was available. Selected scans were all those from males and females who, according to self-report, lack a personal or family history of developmental disorders, twinning, or neurological conditions that are known to alter brain morphology from normal. The characteristics of the individuals from whom these scans were obtained are described in Table 3. Scans included an axial view set at a similar angle as the scans from subjects in this study.

Scans were clinically evaluated by a neuroradiologist prior to quantitative analysis. No parenchymal lesions were
Figure 1. Sagittal reconstruction of slices comprising area measures

SF = Superior frontal area; MF = Middle frontal area; IF = Inferior frontal region;
PSA = Perisylvian area; ST = Superior temporal area; MT = Middle temporal area;
SM/Ang = Supramarginal/angular area; Occip = Occipital area
Figure 2. Axial views of areas measured at three levels in the brain.
reported for any subject. One comparison scan from a female control was noted to have two punctate regions of hyperintensity in the centrum semiovale on the T2-weighted, axial image. These were not visible on a T1-weighted coronal scan. The scans were dummy coded by a research assistant so that those measuring the scans were unaware of the subject identity or language status. Scans were measured by five assistants who were not familiar with the subjects or hypotheses under study and me.

MRI films from these scans were computer digitized and measured using JAVA software (Jandel Scientific, 1988). The instrumentation used for quantitative analysis is provided in Appendix C. A calibration figure of 300 mm$^2$ was used to establish the degree of measurement error attributable to the resolution of the computer system and human error under optimal conditions. The mean value obtained for this figure was 300.62 mm$^2$ with a standard error of 0.16 mm$^2$. Measurement error under optimal conditions was approximately 0.6 percent.

A series of regional brain volumes was obtained for each subject and control scan. Measures were developed based upon both neuroanatomical divisions visible on the MRI scans and consideration of the time of development for cortical regions (cf. Chi et al, 1977b). The procedures for
measuring each region are given in Appendix D. These regions are illustrated in Figures 1 and 2. All regional measures are expressed as a proportion of total brain size to stabilize the values for differences in head sizes across subjects.

A quotient reflecting the degree of asymmetry or symmetry was calculated for each pair of homologous cerebral areas measured. This quotient corresponds to the right regional volume divided by the left. Asymmetries (right > left or left > right) and symmetry (left = right) are classified with reference to the intertester measurement error for each measure. Perfect symmetry results in a quotient of 1.00. When measurement error is taken into account, asymmetry can be defined as values that exceed values of 1.00 +/-1.64 SE for quotient values.

Measurement reliability was assessed using a Pearson product-moment correlation for each anatomical measure completed. Reliability was assessed for every scan completed for a family member and for at least 20 percent of all comparison scans (selected at random). Acceptable reliability was defined as an r-squared value of .70 (r = .84) and above for a series of measures. The r values for each neuroanatomical region are provided in Table 4.

A pilot study of three SLI boys who served as subjects
in a previous study (Plante et al, 1990) indicated that certain of these brain regions were most likely to be atypical (see Appendix E). These include an asymmetry of the perisylvian area as well as proportional volumes of the superior, middle, and inferior frontal areas, superior and middle temporal areas, occipital areas, supramarginal/angular areas, and perisylvian areas.
Chapter III
RESULTS

Comparison scans

Prior to comparisons with probands and their family members, the anatomical measures for males and females were tested for gender differences. No significant (p < .10, two-tailed test) differences for scans from male and female members of the comparison group were found for either proportional volumes or for degree of asymmetry. Consequently, all comparison scans were grouped together for comparison with probands and their family members. The proportional volumes for each regional measure in the comparison group are reported in Table 4. These values will serve as the reference for evaluating proportional volumes from the scans of family members. The asymmetries for each region are reported in Table 5. In eight of the nine areas measured, no consistent asymmetry was detected for a majority of the comparison scans. The perisylvian area was the one exception (M = 0.92, SD = 0.06). In a majority (n = 10) of comparison scans, a left > right asymmetry was documented, which is the predicted asymmetry based on previous studies (Chi, Dooling, & Gilles, 1977b; Geschwind & Levitsky, 1968; Wada, Clarke, & Hamm, 1975; Witleson &
<table>
<thead>
<tr>
<th></th>
<th>Regional volumes Right</th>
<th></th>
<th>(area/cerebrum)</th>
<th>Reliability</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>SEM</td>
<td>Mean</td>
</tr>
<tr>
<td>Inf. Frontal</td>
<td>0.86</td>
<td>0.20</td>
<td>0.08</td>
<td>0.84</td>
</tr>
<tr>
<td>Mid. Frontal</td>
<td>1.41</td>
<td>0.39</td>
<td>0.14</td>
<td>1.43</td>
</tr>
<tr>
<td>Sup. Frontal</td>
<td>1.82</td>
<td>0.43</td>
<td>0.13</td>
<td>1.77</td>
</tr>
<tr>
<td>Mid. Temporal</td>
<td>1.16</td>
<td>0.33</td>
<td>0.07</td>
<td>1.15</td>
</tr>
<tr>
<td>Sup. Temporal</td>
<td>1.61</td>
<td>0.37</td>
<td>0.08</td>
<td>1.51</td>
</tr>
<tr>
<td>Perisylvian</td>
<td>1.82</td>
<td>0.21</td>
<td>0.06</td>
<td>1.97</td>
</tr>
<tr>
<td>Supramar/Ang.</td>
<td>1.25</td>
<td>0.26</td>
<td>0.09</td>
<td>1.22</td>
</tr>
<tr>
<td>Occipital</td>
<td>3.75</td>
<td>0.66</td>
<td>0.16</td>
<td>3.86</td>
</tr>
<tr>
<td>Hemispheres</td>
<td>49.51</td>
<td>0.01</td>
<td>0.001</td>
<td>50.49</td>
</tr>
</tbody>
</table>
Table 5.
Asymmetries and symmetries* from comparison scans.

<table>
<thead>
<tr>
<th>Region</th>
<th>Asymmetry Mean</th>
<th>L &gt; R</th>
<th>L = R</th>
<th>R &gt; L</th>
<th>Symmetry criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inf. Frontal</td>
<td>1.06</td>
<td>0</td>
<td>14</td>
<td>3</td>
<td>1.00 +/-0.24</td>
</tr>
<tr>
<td>Mid. Frontal</td>
<td>0.99</td>
<td>1</td>
<td>14</td>
<td>2</td>
<td>1.00 +/-0.18</td>
</tr>
<tr>
<td>Sup. Frontal</td>
<td>1.04</td>
<td>5</td>
<td>5</td>
<td>7</td>
<td>1.00 +/-0.05</td>
</tr>
<tr>
<td>Mid. Temporal</td>
<td>1.01</td>
<td>3</td>
<td>11</td>
<td>2</td>
<td>1.00 +/-0.14</td>
</tr>
<tr>
<td>Sup. Temporal</td>
<td>1.07</td>
<td>0</td>
<td>13</td>
<td>4</td>
<td>1.00 +/-0.18</td>
</tr>
<tr>
<td>Perisylvian</td>
<td>0.92</td>
<td>10</td>
<td>7</td>
<td>0</td>
<td>1.00 +/-0.05</td>
</tr>
<tr>
<td>Supramar/Ang.</td>
<td>1.05</td>
<td>0</td>
<td>14</td>
<td>3</td>
<td>1.00 +/-0.22</td>
</tr>
<tr>
<td>Occipital</td>
<td>0.98</td>
<td>3</td>
<td>13</td>
<td>1</td>
<td>1.00 +/-0.07</td>
</tr>
<tr>
<td>Hemispheres</td>
<td>1.02</td>
<td>1</td>
<td>11</td>
<td>5</td>
<td>1.00 +/-0.03</td>
</tr>
</tbody>
</table>

*Symmetry is set at 1.64(SEM) for each measure of asymmetry.
Pallie, 1973). Because a left equals right (L = R) configuration was the less frequent configuration, it will be referred to as "atypical." Likewise, because right > left configuration was not seen in the comparison group, this configuration will also be referred to as "atypical."

**Subject scans**

**Perisylvian asymmetries**

Table 6 displays the perisylvian quotients obtained for individual members of each family. As for comparison scans, quotients of 1.00 +/-0.05 correspond to a judgement of symmetry.

**Parents**

Atypical perisylvian asymmetries were documented in seven of the eight parents (M = 1.04, SD = 0.10). The probability of these asymmetries occurring by chance, based on the rate of perisylvian symmetry among comparison scans is .016. The difference between the distributions of perisylvian asymmetries from parent and comparison scans was statistically significant as well (t = 3.73, df = 23; p < .01). This finding reflects the fact that the perisylvian asymmetry distribution from comparison scans ranged from L > R (n = 11) to L = R (n = 7) configurations, whereas the parents had a range of configurations that extended from L >
<table>
<thead>
<tr>
<th>Family</th>
<th>Quotient</th>
<th>Configuration</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mother</td>
<td>1.06</td>
<td>R &gt; L</td>
<td>atypical</td>
</tr>
<tr>
<td>father</td>
<td>1.19</td>
<td>R &gt; L</td>
<td>atypical</td>
</tr>
<tr>
<td>sibling-1</td>
<td>0.95</td>
<td>R = L</td>
<td>atypical</td>
</tr>
<tr>
<td>sibling-2</td>
<td>1.02</td>
<td>R = L</td>
<td>atypical</td>
</tr>
<tr>
<td>proband</td>
<td>0.83</td>
<td>L &gt; R</td>
<td>typical</td>
</tr>
<tr>
<td>Family 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mother</td>
<td>0.96</td>
<td>L = R</td>
<td>atypical</td>
</tr>
<tr>
<td>father</td>
<td>1.16</td>
<td>R &gt; L</td>
<td>atypical</td>
</tr>
<tr>
<td>sibling</td>
<td>0.82</td>
<td>L &gt; R</td>
<td>typical</td>
</tr>
<tr>
<td>proband</td>
<td>0.91</td>
<td>L &gt; R</td>
<td>typical</td>
</tr>
<tr>
<td>Family 3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mother</td>
<td>1.06</td>
<td>R &gt; L</td>
<td>atypical</td>
</tr>
<tr>
<td>father</td>
<td>1.04</td>
<td>R = L</td>
<td>atypical</td>
</tr>
<tr>
<td>sibling</td>
<td>0.95</td>
<td>R = L</td>
<td>atypical</td>
</tr>
<tr>
<td>proband</td>
<td>1.01</td>
<td>R = L</td>
<td>atypical</td>
</tr>
<tr>
<td>Family 4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mother</td>
<td>0.99</td>
<td>R = L</td>
<td>atypical</td>
</tr>
<tr>
<td>father</td>
<td>0.88</td>
<td>L &gt; R</td>
<td>typical</td>
</tr>
<tr>
<td>proband</td>
<td>1.10</td>
<td>R &gt; L</td>
<td>atypical</td>
</tr>
<tr>
<td>sibling</td>
<td>0.81</td>
<td>L &gt; R</td>
<td>typical</td>
</tr>
</tbody>
</table>

* asymmetries of within 1.00 +/-0.05 are classified as L = R
R (n = 1) through L = R (n = 4) to R > L (n = 3).

Probability levels calculated separately for mothers and for fathers are useful to evaluate whether either mothers or fathers alone produce a statistically significant finding. All mothers had atypical perisylvian asymmetries (p = .029; two having a L = R configuration and two having a R > L configuration. Fathers in Families 1, 2, and 3 also had atypical perisylvian asymmetries (p = .279).

Conditional probabilities (Fleiss, 1981) describe the degree to which atypical perisylvian asymmetries are likely to be found in mothers and in fathers whose spouses have the trait. Although the sample studied here is small, this probability provides an estimate of the degree of concordance for perisylvian asymmetries among parents that may be useful in future studies. Because all mothers had atypical perisylvian asymmetries, the conditional probability for atypical perisylvian asymmetries in mothers when fathers have the trait is 1.00. The probability of a father having atypical perisylvian asymmetry when the spouse has the trait is .75.

**Probands and Siblings**

Two probands also had atypical perisylvian configurations (one each L = R, R > L). These probands belonged to families 3 and 4. Because proband-1 was the
subject of another study (Plante et al., 1990), his perisylvian configuration \((L > R)\) was known prior to his inclusion in this study. Therefore, he was excluded in all probability calculations involving the perisylvian areas. The remaining three probands are too few in number to produce statistically significant probability levels.

Four of the five siblings also had atypical perisylvian configurations \((L = R\) in all cases). No probability level is given for this rate because the sibling data are dependent.

An over-all conditional probability for offspring of parents with atypical perisylvian asymmetry was calculated. This probability describes the degree to which atypical perisylvian asymmetries in parents are associated with the same trait in children. When at least one parent has an atypical perisylvian asymmetry, the likelihood of at least one offspring having the trait is .75. The likelihood of the proband having the trait is .66. (Proband-1 has been excluded from this calculation.)

Proportional volumes

Proportional volumes (displayed in Tables 7 - 10) were obtained for eight cerebral areas in the left and right hemisphere in order to document the pattern of cortical
Table 7.
Z-scores for proportional volumes for eight cerebral areas in members of Family-1.

<table>
<thead>
<tr>
<th>Area</th>
<th>Mother</th>
<th>Father</th>
<th>Sib-1</th>
<th>Sib-2</th>
<th>Proband</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>rt</td>
<td>lf</td>
<td>rt</td>
<td>lf</td>
<td>rt</td>
</tr>
<tr>
<td>Superior Frontal</td>
<td>-2.10</td>
<td>-1.56</td>
<td>-0.98</td>
<td>-1.11</td>
<td>-0.55</td>
</tr>
<tr>
<td>Middle Frontal</td>
<td>-1.38</td>
<td>-1.75</td>
<td>-0.21</td>
<td>-0.78</td>
<td>-0.15</td>
</tr>
<tr>
<td>Inferior Frontal</td>
<td>-0.61</td>
<td>-0.13</td>
<td>-1.31</td>
<td>-0.98</td>
<td>0.53</td>
</tr>
<tr>
<td>Perisylvian</td>
<td>2.10</td>
<td>0.81</td>
<td>2.19</td>
<td>-0.33</td>
<td>2.04</td>
</tr>
<tr>
<td>Superior Temporal</td>
<td>0.72</td>
<td>0.38</td>
<td>-1.80</td>
<td>1.86</td>
<td>0.96</td>
</tr>
<tr>
<td>Middle Temporal</td>
<td>2.78</td>
<td>2.43</td>
<td>0.58</td>
<td>0.04</td>
<td>2.53</td>
</tr>
<tr>
<td>Supramarginal/Angular</td>
<td>0.52</td>
<td>1.45</td>
<td>0.86</td>
<td>0.39</td>
<td>1.03</td>
</tr>
<tr>
<td>Occipital</td>
<td>0.39</td>
<td>0.54</td>
<td>-1.17</td>
<td>-1.25</td>
<td>-0.23</td>
</tr>
</tbody>
</table>

Underlined values are those for which z equals or exceeds +/-1.64 (p < .10, two-tailed test)
Bolded values are those for which z equals or exceeds +/-1.96 (p < .05, two-tailed test)
<table>
<thead>
<tr>
<th></th>
<th>Mother</th>
<th></th>
<th>Father</th>
<th></th>
<th>Sib</th>
<th></th>
<th>Proband</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>rt</td>
<td>lf</td>
<td>rt</td>
<td>lf</td>
<td>rt</td>
<td>lf</td>
<td>rt</td>
<td>lf</td>
</tr>
<tr>
<td>Superior Frontal</td>
<td>0.53</td>
<td>1.17</td>
<td>-1.24</td>
<td>-1.24</td>
<td>2.39</td>
<td>3.03</td>
<td>-0.24</td>
<td>0.39</td>
</tr>
<tr>
<td>Middle Frontal</td>
<td>0.77</td>
<td>0.40</td>
<td>0.04</td>
<td>-0.67</td>
<td>2.48</td>
<td>1.91</td>
<td>0.96</td>
<td>0.35</td>
</tr>
<tr>
<td>Inferior Frontal</td>
<td>2.24</td>
<td>1.04</td>
<td>-0.33</td>
<td>-0.14</td>
<td>1.26</td>
<td>0.72</td>
<td>-0.49</td>
<td>0.28</td>
</tr>
<tr>
<td>Perisylvian</td>
<td>-0.86</td>
<td>-1.38</td>
<td>0.80</td>
<td>-1.34</td>
<td>-0.59</td>
<td>0.52</td>
<td>0.03</td>
<td>0.57</td>
</tr>
<tr>
<td>Superior Temporal</td>
<td>-1.39</td>
<td>-1.59</td>
<td>-1.69</td>
<td>-1.63</td>
<td>-1.27</td>
<td>-1.32</td>
<td>-1.81</td>
<td>-2.10</td>
</tr>
<tr>
<td>Middle Temporal</td>
<td>-1.65</td>
<td>-1.30</td>
<td>0.18</td>
<td>0.04</td>
<td>-2.41</td>
<td>-2.33</td>
<td>-0.40</td>
<td>-0.35</td>
</tr>
<tr>
<td>Supramarginal/Angular</td>
<td>0.93</td>
<td>0.30</td>
<td>-0.13</td>
<td>-1.05</td>
<td>1.67</td>
<td>0.81</td>
<td>1.57</td>
<td>0.09</td>
</tr>
<tr>
<td>Occipital</td>
<td>1.26</td>
<td>1.62</td>
<td>0.10</td>
<td>0.11</td>
<td>-1.55</td>
<td>-1.18</td>
<td>1.07</td>
<td>0.92</td>
</tr>
</tbody>
</table>

Underlined values are those for which z equals or exceeds +/-1.64 (p < .10, two-tailed test)

Bolded values are those for which z equals or exceeds +/-1.96 (p < .05, two-tailed test)
Table 9.
Z-scores for proportional volumes for eight cerebral areas in members of Family-3.

<table>
<thead>
<tr>
<th>Area</th>
<th>Mother</th>
<th>Father</th>
<th>Sib</th>
<th>Proband</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>rt</td>
<td>lf</td>
<td>rt</td>
<td>lf</td>
</tr>
<tr>
<td>Superior Frontal</td>
<td>-0.64</td>
<td>-0.31</td>
<td>1.62</td>
<td>1.58</td>
</tr>
<tr>
<td>Middle Frontal</td>
<td>-0.08</td>
<td>-0.52</td>
<td>0.23</td>
<td>-0.01</td>
</tr>
<tr>
<td>Inferior Frontal</td>
<td>0.19</td>
<td>0.21</td>
<td>1.67</td>
<td>0.62</td>
</tr>
<tr>
<td>Perisylvian</td>
<td>0.19</td>
<td>-1.11</td>
<td>-0.03</td>
<td>-1.17</td>
</tr>
<tr>
<td>Superior Temporal</td>
<td>-1.00</td>
<td>-1.21</td>
<td>-3.05</td>
<td>-3.83</td>
</tr>
<tr>
<td>Middle Temporal</td>
<td>1.35</td>
<td>0.84</td>
<td>0.84</td>
<td>1.86</td>
</tr>
<tr>
<td>Supramarginal/Angular</td>
<td>0.47</td>
<td>0.44</td>
<td>1.81</td>
<td>0.88</td>
</tr>
<tr>
<td>Occipital</td>
<td>1.62</td>
<td>1.86</td>
<td>0.45</td>
<td>0.62</td>
</tr>
</tbody>
</table>

Underlined values are those for which z equals or exceeds +/-1.64 (p < .10, two-tailed test)
Bolded values are those for which z equals or exceeds +/-1.96 (p < .05, two-tailed test)
Table 10.  
Z-scores for proportional volumes for eight cerebral areas in members of Family-4.

<table>
<thead>
<tr>
<th>Area</th>
<th>Mother</th>
<th>Father</th>
<th>Proband</th>
<th>Sib</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>rt</td>
<td>lf</td>
<td>rt</td>
<td>lf</td>
</tr>
<tr>
<td>Superior Frontal</td>
<td>-0.95</td>
<td>-0.73</td>
<td>1.64</td>
<td>0.89</td>
</tr>
<tr>
<td>Middle Frontal</td>
<td>-0.65</td>
<td>-0.09</td>
<td>1.00</td>
<td>0.32</td>
</tr>
<tr>
<td>Inferior Frontal</td>
<td>0.43</td>
<td>0.12</td>
<td>-1.22</td>
<td>-0.38</td>
</tr>
<tr>
<td>Perisylvian</td>
<td>-0.89</td>
<td>-1.68</td>
<td>1.74</td>
<td>2.72</td>
</tr>
<tr>
<td>Superior Temporal</td>
<td>-1.24</td>
<td>-1.68</td>
<td>1.00</td>
<td>1.52</td>
</tr>
<tr>
<td>Middle Temporal</td>
<td>-1.55</td>
<td>-1.64</td>
<td>-0.46</td>
<td>-0.13</td>
</tr>
<tr>
<td>Supramarginal/Angular</td>
<td>0.54</td>
<td>0.47</td>
<td>-0.70</td>
<td>-1.03</td>
</tr>
<tr>
<td>Occipital</td>
<td>-0.43</td>
<td>-0.27</td>
<td>0.91</td>
<td>1.90</td>
</tr>
</tbody>
</table>

Underlined values are those for which z equals or exceeds +/-1.64 (p < .10, two-tailed test)
Bolded values are those for which z equals or exceeds +/-1.96 (p < .05, two-tailed test)
involvement. Proportional volumes for the perisylvian area are useful in that they illucidate the nature of atypical perisylvian asymmetries. Proportional volumes in additional cerebral regions describe the extent to which atypical effects on the brain can be found outside the perisylvian areas. The proportional volumes for each subject were converted to z-scores so that they may be evaluated relative to the range seen in the comparison group.

With the use of a stringent criteria for deviance (p < .05, two-tailed test), no more than one deviant z-score was obtained for any area in the left or right hemisphere in comparison scans. For family members, at least one deviant z-score was documented for every region measured, with the exception of the supramarginal/angular gyrus area. The number of family members with deviant z-scores exceeded, by at least one, the number of deviant z-scores in the comparison group for the perisylvian, superior temporal, and middle temporal areas.

The right perisylvian areas, for members of three families (1, 3, & 4), were significantly larger (p < .05, two tailed) than those from comparison scans. The left perisylvian was significantly larger than in the comparison scans for members of two families (1 & 4). No statistical comparison can be made for these data due to data dependency.
among family members.

For the middle temporal area, z-scores for at least one member of each family were significantly different compared with the distribution of the comparison group. In all cases, deviant z-scores were obtained bilaterally. In most cases, the middle temporal areas were significantly smaller than those obtained from comparison scans. Family 1 included two members for whom this area was significantly larger than expected while one member showed the opposite effect (significantly smaller).

For the superior temporal area and the superior frontal area, members of two families had significantly deviant z-scores unilaterally or bilaterally. This number of subjects exceeds the number in the comparison group by one for both areas.

The use of a less stringent requirement for deviancy (p < .10, two-tailed test), increased the discrepancy between number of deviant z-scores found for subjects and in the comparison group for each of the areas identified above. This discrepancy in the z-score distributions between subjects and comparisons provides converging evidence for a stable neuroanatomical effect in the areas identified.
Neuroanatomical variability within families

Marked variability was noted for the neuroanatomical profiles within each of the families. Figure 3 illustrates that the range of perisylvian quotients in each family overlapped the range documented in the comparison group. In addition, at least one quotient that was outside the range in the comparison group was documented in every family. In three of the families, the range seen in biologically related individuals exceeded the range documented for the unrelated individuals who served as comparisons. The ranges of perisylvian asymmetries obtained for the four families were not markedly different.

Similarly, there was notable variability for the rates of deviant proportional volumes among family members, as seen in Tables 7 - 10. In areas were deviant z-scores from subjects exceeded those from the comparison group, deviant scores tended to be distributed across the different families.

Association of atypical neuroanatomy and impaired language

Perisylvian asymmetries

Figure 4 illustrates the family constellations of perisylvian findings (typical or atypical) in relation to indications of language impairment in each family member.
Figure 3. 
Range of perisylvian asymmetries in the comparison group and in members of families of language-disordered boys.

<table>
<thead>
<tr>
<th>Perisylvian Classification</th>
<th>L &gt; R</th>
<th>L = R</th>
<th>R &gt; L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perisylvian Quotients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.80</td>
<td>0.85</td>
<td>0.90</td>
<td>0.95</td>
</tr>
</tbody>
</table>

Comparison group: * ** * ***** * * * *** *

Family 1: P S S M F
Family 2: S P M F
Family 3: S P F M
Family 4: S F M P

F = father; M = mother; P = proband; S = sibling
Figure 4. Constellations of atypical perisylvian asymmetry and history of communication difficulty in four families.

- Communication difficulty
- Atypical perisylvian asymmetry

P: proband
NS: Not scanned
Several measures are available to describe the association between atypical perisylvian asymmetries and evidence of impaired language. This association will be considered separately for parents and for children because different methods were used to determine history of childhood language impairment in these two groups of subjects.

Parents

Parents were considered to have a history of early communication difficulty if they self-reported any of the following characteristics: early speech or language difficulty, difficulty with reading, or academic failure (cf. Tallal, Ross, & Curtis, 1989a & b). One method that describes the relation between these factors and perisylvian asymmetry is a measure of the relative "sensitivity" (Fleiss, 1981, p. 6) of a history of communication difficulty as an indicator of the presence of atypical perisylvian asymmetries in parents. The conditional probability that describes sensitivity is .86.

The converse of the sensitivity of a measure is its "specificity" (Fleiss, 1981, p. 6). A proportional probability for specificity describes the degree to which atypical perisylvian asymmetries are specific to individuals with a history of communication difficulties. When parents who reported communication difficulties are compared with
comparisons who lack such a history, the specificity level is .59.

A third method to describe the relation between atypical perisylvian asymmetries and a history of communication difficulty is a "proportion of attributable risk" (Fleiss, 1981, p.75). This statistic estimates the proportion of the probability of having a given condition that can be attributed to the presence of a precursor condition. It is used to estimate the degree to which early communication difficulty is attributable to the presence of atypical perisylvian asymmetries in the combined set of parents and the comparison group. The proportion of attributable risk estimated from both the parents and the comparison group is .74. This value probably underestimates attributable risk in parents of language-impaired children due to the fact that the rate of the risk factor (atypical perisylvian asymmetries) is significantly higher in this population than in the normal population (Fleiss, 1981, p. 76).

**Siblings**

Most of the siblings studied had impaired language as documented by standardized testing. Three of the siblings with impaired language also had atypical perisylvian areas (families 1 & 4). A fourth sibling, in family 3, had
atypical perisylvian asymmetry without a documented language impairment. The statistical procedures used with parents to describe the relation between language impairment and atypical perisylvian asymmetries require independent selection of cases. Therefore, they cannot be applied to data from siblings.

**Proportional volumes**

**Parents**

The mother in Family 1 had deviant z-scores in the superior frontal gyrus region and in the middle temporal gyrus region. This parent also had a history of communication difficulty. The conditional probability of deviant z-scores in either area given a history of communication difficulty is .14. No other region was tested using conditional probabilities because deviant scores occurred with equal frequency in parent and comparison scans.

**Probands and Siblings**

For the middle temporal gyrus region, one proband (in Family 1) and four siblings (one in each family) had significantly deviant z-scores. Three of the siblings also had a documented language impairment. For the superior
temporal gyrus region, one proband (in Family 2) had a deviant z-score. No language impairment was documented for this child. One sibling (in Family 2) without documented language impairment also had a deviant z-score in the superior frontal gyrus region.
CHAPTER 4
DISCUSSION

Perisylvian findings

Atypical perisylvian asymmetries were documented in seven of eight parents of SLI boys. This statistically significant finding establishes that a neuroanatomical effect previously associated with SLI in boys (Plante et al, 1990) is also found among the parents of such children. The majority of these parents also had children with atypical perisylvian asymmetries. Thus atypical perisylvian asymmetries appeared in two generations within families that have a history of language disorder.

In five cases, the atypical perisylvian asymmetries occurred because the right perisylvian areas were larger than expected, in relation to total brain size while the left perisylvian area was of the expected proportional size. For these subjects, this perisylvian configuration did not vary with the type of atypical perisylvian asymmetry; a large right perisylvian area occurred in the presence of both right > left and right = left perisylvian asymmetries. A sixth subject had perisylvian areas that were larger than expected bilaterally, which produced perisylvian symmetry. One subject had a left perisylvian area that was
disproportionately large while the right was of the expected size. In this subject, this pattern produced the typical left > right asymmetry. Larger than typical volumes provide strong evidence that an effect altered cerebral development, rather than damaged a brain that had developed normally. This pattern of results has been previously reported for an SLI boy (Plante et al, 1989) and for four males who had developmental dyslexia (Galaburda et al, 1985). In the present study, this pattern occurred for both parents and children who had atypical perisylvian asymmetries. Thus atypical perisylvian findings, which differed in degree of asymmetry across subjects, were qualitatively similar in terms of proportional volume.

Perisylvian-language relations

The assumption that perisylvian abnormalities are linked to developmental language disorders is supported from both data-based and theoretical positions. Models based on anatomical correlates of acquired language disorders highlight the importance of left hemisphere perisylvian structures (e.g. Geschwind, 1979). As discussed above, previous reports have linked developmentally impaired language to disturbances to the cellular architectonics (Cohen et al, 1988; Galaburda et al, 1985) and in

The relation between developmental language disorders and atypical perisylvian configurations is further supported by the self-reported histories of the parents who were studied. Most parents reported problems indicative of early communication difficulty and possible language disorder. Communication difficulty was defined as a reported childhood difficulty with speech or language, academic failure, or difficulty with reading (cf. Tallal et al, 1989a & b). When parents reported such difficulty, the probability of their having atypical perisylvian configurations was relatively high (.86), indicating that such a history is a sensitive indicator of the presence of an atypical brain.

Because some individuals who did not report a history of communication difficulty also had atypical perisylvian asymmetries, this neuroanatomical marker, as measured by MRI, cannot be considered specific to language disorder alone. However, the relation is sufficiently strong as to suggest that the atypical perisylvian asymmetries represent a risk factor that increases the likelihood (p = .74) that an individual will experience difficulty with communication skills. These data suggest that perisylvian asymmetries
reflect biological factors that place some families at risk for language disorder. The notion of familial risk is supported by the multiple cases of language disorder within families as well as the indications of similar problems in parents and their children.

**Language disorder as a transmitted effect**

The results of this study are consistent with the hypothesis that a transmittable, biological effect contributes to the expression of a developmental language disorder. Support for this hypothesis requires a demonstration that the behavioral and biological characteristics both occur across generations within families, and both are associated within individual members of families. Finding atypical perisylvian asymmetries in parents and their children establishes that this biological marker occurs across generations in families affected by language disorder. Likewise, indications of impaired language, based on testing in children and self-report in adults, also occurred across generations in these families. Finally, the rate of both the biological and behavioral factors suggests that a proportion of the risk for communication difficulty can be attributed to the presence of atypical perisylvian asymmetries. Thus, atypical
perisylvian asymmetries have been linked with the behavioral disorder in the present study and both appear to be transmitted from parents to children in the families of SLI boys.

The results of this study confirm and extend previous behavioral studies that examine the issue of transmission of language disorder through families. The high prevalence of early communication difficulties among the parents is consistent with previous studies that used self report of communication difficulty to establish the prevalence of possible language disorder among parents of language-impaired children (Byrne et al, 1974; Neils & Aram, 1986; Tallal et al, 1989a & b; Tomblin, 1989). The findings of the present study extend previous reports by pairing self report with a neuroanatomical correlate of language disorder which is unknown to the parents. The relatively high agreement between neuroanatomical and behavioral features provide converging evidence that the high rate of communication difficulties reported for parents is not the sole result of over-reporting by parents.

Previous studies have suggested that fathers of language-impaired children are more likely than mothers to indicate signs of disorder in themselves (Neils & Aram, 1986; Tallal et al, 1989a & b). In this study, one more
father than mother reported signs of communication difficulties. In contrast, one more mother than father had atypical perisylvian asymmetries. Because the majority of mothers and fathers had both atypical perisylvian asymmetries and behavioral indicators of language disorder, this study does not provide clear evidence concerning the mode of transmission of these features. The relatively high concordance between spouses for atypical perisylvian asymmetries in this small sample indicates future studies must have a relatively large sample size in order to assess the relative contribution to the transmission of language disorder by either mothers or fathers.

Like the high rate of communication difficulty among the parents studied, the high rate of language disorder among the siblings of SLI boys is not unusual, according to reports in the literature (Bishop & Edmundson, 1986; Neils & Aram, 1986; Tallal et al., 1989a & b; Tomblin, 1989). Unlike previous studies of familial constellation of language disorder, in the present study language impairment in siblings was determined by standardized testing rather than by parental report. Siblings who evidenced significantly impaired language also had atypical perisylvian asymmetries. Thus, the data for siblings, who were not selected for study on the basis of language scores, suggest that the presence
of language disorder is predictive of the presence of atypical perisylvian asymmetries.

In one sibling's case, atypical perisylvian asymmetries were documented in the absence of evidence for impaired language. This dissociation was previously documented in a normally developing twin of an SLI boy (Plante et al., 1989). A percentage of individuals without a personal history of impaired language also have atypical perisylvian asymmetries. The presence of atypical perisylvian asymmetries without a documented language disorder suggest that atypical perisylvian asymmetries are not in themselves sufficient for the expression of language disorder, but are compatible with the notion of familial risk.

A neuroanatomical effect that occurs across generations within the same family is unlikely to be the result of accidental events such as trauma or toxins. The kind of evidence that would advance trauma or toxins as potential explanations of the perisylvian effects was lacking in this group of subjects. For example, brain damage would be expected either to leave visibly detectable evidence (e.g. parenchymal lesions, ventricular enlargement), or measurable decreases in the perisylvian volumes due to tissue loss. No evidence of damage was reported during routine clinical examination of MRI scans. More importantly, perisylvian
volumes were not smaller but larger than usual in many cases. As mentioned previously, this is the opposite effect that damage would be expected to produce.

Although not tested exhaustively, toxins appear to be an unlikely explanation as well. A toxin would have to act during prenatal development to explain the perisylvian findings. Responses to case histories identified only one potential toxin, parental exposure to cigarette smoke, that occurred across families. Since this factor occurred in the comparison group as well, it cannot be considered unique to language-disordered individuals. The likelihood of an unreported, environmental toxin accounting for the perisylvian findings is reduced by the fact that parents and offspring in each family were born in different parts of the country.

Tomblin (1989) has hypothesized that multiple cases of language disorder within families might be explained by poor rearing practices. The present findings are incompatible with this hypothesis as atypical perisylvian asymmetries reflect prenatal effects. Although environmental input will influence cellular connections (see Cowan, 1979 for examples), input does not change gyral configurations at the level of gross anatomy. Thus, less than optimal language experiences could not account for the atypical neuroanatomy
observed. The presence of a prenatal neuroanatomical effect rules out parental rearing practices as a potential causal factor, although they may be maintaining factors in the expression of developmental language disorder in some cases.

Range of neuroanatomical effect

Variability of neuroanatomical findings across language-disordered children may signal a range of effect produced by a single cause, or different causes. Because of the similarity among genetically related family members for biological background, the range of neuroanatomical findings among family members is likely to reflect the effects of similar biological factors. Considered in this context, the range of neuroanatomical findings within the families studied can serve as a benchmark for evaluating neuroanatomical heterogeneity across unrelated language-impaired individuals. It is therefore notable that the ranges for perisylvian quotients among related family members were broader than the range seen in the comparison group for three of the four families studied. This suggests that relatively similar biological backgrounds are associated with substantial neuroanatomical variability.

The perisylvian quotients did not appear to be sensitive to the degree of language disorder across members
of the four families. For example, the sibling in Family 3, who lacks a documented language disorder, has a higher quotient than either of the probands in Families 1 and 2. Part of the reason for the apparent insensitivity of the degree of perisylvian asymmetry to the degree of behavioral disorder is related to the limits of MRI as a tool for documenting neuroanatomical effects. As mentioned in the introduction, MRI detects only deviations in gross anatomy. This characteristic of MRI can result in effects that seem counter-intuitive. For example, in many of the subjects studied, the proportional volumes for the left perisylvian areas were of the expected size while the right tended to be significantly larger than expected. This pattern of findings has been previously documented for the perisylvian area in an SLI boy (Plante et al, 1989) and for the plana temporale in dyslexic subjects (Galaburda et al, 1985).

This pattern appears to be contradictory to the brain-language relations documented in cases of acquired language disorders which are associated with unilateral lesions of the left perisylvian area. However, microscopic examination of the brains of dyslexics revealed cellular disturbances predominantly in the left perisylvian area (Galaburda et al, 1985). Thus, examination of gross anatomy, the level detectable with MRI, implicated the opposite side of the
brain compared with examination of cellular anatomy in the same subjects. The implications of this limitation of MRI as a tool is that many forms and combinations of cellular-level effects will not produce a detectable effect at the level of gross anatomy. This limitation probably also contributes to the apparent range of neuroanatomical effects among family members.

Pattern of cerebral involvement

The idea of a range of neuroanatomical effect is again reflected by the data indicating neuroanatomical involvement outside of the perisylvian areas. Although in every family, atypical proportional volumes were obtained for every member, the areas so identified varied across family members. Some cerebral areas were more frequently deviant than others across both individual subjects and across families. These included, along with the perisylvian areas, the superior frontal, superior temporal, and middle temporal areas.

The most frequently obtained deviant proportional volumes were for the left and right middle temporal area. This area tended to be smaller than expected, compared with control scans. In all cases, when deviant scores were obtained, they were obtained bilaterally. This is clear
evidence of bilateral involvement in the subjects studied. This is not unexpected, as an effect on the developing brain is likely to affect both the left and right hemispheres. Indeed, autopsy studies of individual with disorders that included impaired language have revealed bilateral cellular-level abnormalities (Galaburda et al, 1985; Landau et al, 1960).

Other deviant proportional volumes were obtained in the superior temporal area and superior frontal area. In both cases, both disproportionately large and disproportionately small volumes were obtained across subjects. Such scores were obtained unilaterally and bilaterally. Findings in spatially disparate regions such as the superior frontal and perisylvian areas provide evidence of widespread cerebral involvement associated with developmental language disorder. This neuroanatomical feature, like bilateral involvement is not unexpected since an in-utero effect is likely to affect all brain areas, to varying extents.

Because gyral patterns are determined during the prenatal period of cell migration (see Cowan, 1979 for an overview of cerebral development), disturbances in the size or configuration of gyri are likely to reflect an alteration in cerebral development. The fact that neuroanatomical areas were both significantly larger and smaller than
expected across family members may reflect an interaction between the stage of brain development and the agent(s) producing the neuroanatomical effect (Galaburda et al, 1985; Plante et al, 1989). It is also the case, as discussed previously, that certain combinations of adverse developmental effects will not result in a cerebral effect that is detectable at the level of gross anatomy.

An effect that occurs early, relative to gyral development, would be expected to interfere with the period of cell genesis and migration for that gyrus. If cell genesis or migration is limited, the predicted effect would be a smaller than usual gyral volume. An effect that interferes primarily with the next stage of cerebral development, programmed cell death, would result in gyral regions that are abnormally large. In the normally developing brain many more cells are generated and migrate than are needed. Excess cells, including misplaced and nonfunctional cells, are eliminated during a period of cell death (see Cowan, Fawcett, O'Leary, & Stanfield, 1984 for a review of regressive events in neurogenesis). As stated previously, the strongest evidence from this study for an effect that interacts with brain development comes from the finding of disproportionately large cerebral areas as in the perisylvian areas. Such a finding could not be explained by
damage to a brain that had otherwise developed normally, but is consistent with a failure of regressive events. The presence of neuronal ectopias documented in dyslexic subjects (Galaburda et al, 1985) also suggests a failure of the regressive events that normally eliminate heterotopic cells. In addition, the presence and location of such cells suggest an effect operated on cell migration as well as cell survival.

Given evidence for a developmental effect, the areas that were most often atypical in the subjects studied can be used to hypothesize about the course of altered cerebral development. One approach is to consider the regions where a neuroanatomical effect was documented relative to the time course of gyral development. According to data presented by Chi and colleagues, (1977b) (see Figure 5), the gyral regions most frequently implicated in this study are neither the earliest or latest to appear. The superior temporal gyrus was first identified in 25-50% of the brains studied during the 23 week of gestation. The superior frontal gyrus and middle temporal gyrus followed at 25 and 26 weeks respectively. The perisylvian area covers several regions that are first identified between 23 to 31 weeks.

An inter-hemispheric difference exists for development of three of these four areas. In each case, the gyri appear
Figure 5. Time course of prenatal gyral development

* indicates areas for which gyri in the left hemisphere appear after the homologous gyri in the right hemisphere.

1 based on Chi, Dooling, & Gilles, 1977b.
later in the left hemisphere than in the right. Only one other cerebral region has such an inter-hemispheric difference in the course of development. This is the area of the supramarginal and angular gyri, which first appears at 28 weeks gestation. It has been suggested that such left-right differences leave areas of the left hemisphere more vulnerable to adverse effects on development, compared with the homologous areas in the right hemisphere (Geschwind & Behan, 1982). It is also possible that the interhemispheric difference in the time of development increased the probability that alterations in cerebral development would result in an effect detectable by MRI in one or the other hemisphere.

Unlike the majority of areas that were most often atypical in the family members studied, no left-right difference in development was reported by Chi et al (1977b) for the middle temporal gyrus. The pattern of deviant proportional volumes for this area presents clear evidence of a bilateral effect on brain development. Findings for this area were always similar across hemispheres within any given subject. This similarity across hemispheres is consistent with the fact that these areas develop at the same rate and should be equally affected by any adverse effects.
Hormones as a contributing agent

One potentially transmittable factor, which may or may not be genetically mediated, is gonadal hormones. As reviewed in the introduction, a variety of studies of language- and learning-disabled subjects suggest a hormonal role in the origins of these disorders (Galaburda et al., 1985; Geschwind & Behan, 1982; Plante et al., 1989; Tallal et al., 1989b). Likewise, the action of gonadal hormones may explain the cerebral effects and certain aspects of background history in the subjects of this study.

One indicator of a possible hormonal role in the transmission of language disorders is the high prevalence of dizygotic twinning (cf. Milham, 1964) among the families studied. This familial characteristic has also been documented in previous studies of individuals with impaired language skills (Galaburda et al., 1985; Plante et al., 1989; Plante et al., 1990). The presence of dizygotic twinning in the family history suggests ambient conditions existed that increased the likelihood that family members were exposed to high levels of gonadal hormones in utero. The same ambient conditions would also place other siblings at risk for developmental disorders commonly associated with impaired language. Such conditions would explain the prevalence of
language and learning disorders among the siblings of the probands.

In the absence of evidence for lesion-induced alterations of asymmetries, a hormonally-mediated change in brain development is an attractive explanation for the atypical anatomical findings. Experimental manipulations of either endogenous or exogenous hormone levels alter neuronal volumes in the developing brain (Diamond, Dowling, & Johnson, 1981; Dodson, Shryne, & Gorski, 1988, Gorski, Gordon, Shryne, & Southam, 1978; Jacobson, Csernus, Shryne, & Gorski, 1981; Pappas, Diamond, & Johnson, 1978; Pfaff, 1966; Sandhu, Cook, & Diamond, 1986). Cortical hormone receptors are present during the prenatal period in monkeys (Handa, Connolly, & Resko, 1988; Pomerantz, Fox, Sholl, Vito, & Goy, 1985; Sholl & Kim, 1989;), and in rats (MacLusky, Lieberburg, & McEwen, 1979; McEwen, Plapinger, Chaptal, Gerlach, & Wallach, 1975). These conditions provide an opportunity for hormones to influence cortical development.

One way in which gonadal hormones are known to influence brain development is by increasing survival of cells (Bloch & Gorski, 1988a & b; Dodson et al, 1988; Gorski et al, 1978; Jacobson et al, 1981; Matsumoto & Arai, 1976) and cellular connections (Yu, 1989). Because the presence
of 5 alpha-reductase (which is critical to the conversion of one type of testosterone to an estrogen prior to cellular uptake) increases over the course of gestation in monkeys (Resko, Connolly, & Roselli, 1988), the greatest hormone influence in these areas would be expected during late gestation. A late hormone effect would be predicted to influence cell survival more than cell proliferation or migration. The data from these animal studies demonstrate the potential for gonadal hormones to increase cortical volumes during the prenatal period. Thus, animal models are available that might be applicable to the effects demonstrated in the human subjects of the present study.

Implications for brain-behavior relations in SLI

Current models of brain-language relations reflect information available from the results of lesions to the premorbidly normal, mature brain (e.g. Geschwind, 1979). These models typically emphasize the importance of left perisylvian areas structures and the connecting pathways between these structures and others in cases of acquired language disorder. Studies of acquired language disorders in children (see Aram & Whitaker, 1988 for a review) appear to support the applicability of such models, again emphasizing the importance of perisylvian structures in
cases of acquired language disorder. However, a model of developmentally disordered brain-language relations has not yet been put forward. For purposes of this discussion, a "developmental" disorder will refer to disordered behavior that occurs subsequent to an alteration of brain development. The data from this study indicate a model of developmentally-disordered language would have both similarities and differences with models based on cases of acquired language disorder.

Like models based on acquired language disorders, a model for developmental language disorders would emphasize the importance of the perisylvian areas. In this and previous studies, individuals with developmental disorders that included impaired language had either cellular level pathology (Cohen et al, 1988; Galaburda et al, 1985; Landau et al, 1960) or alterations in the normal pattern of asymmetry for this area (Cohen et al, 1988; Galaburda et al, 1985; Plante et al, 1989; Plante et al, 1990). Because asymmetries of the perisylvian area reflect an asymmetry in the underlying cytoarchitectonic organization (Galaburda & Sanides, & Geschwind, 1978), a disturbance of the asymmetry is likely to reflect altered cytoarchitectonics (e.g. Galaburda et al, 1985). This disturbance may be responsible for the increased difficulty language-disordered children
have in developing the skills that other children seem to master with relative ease. Therefore, although the language-disordered subjects studied to date lack evidence of acquired brain damage to the perisylvian area, a developmental alteration of this cerebral region appears capable of placing these individuals at increased risk for the disorder.

The importance of the perisylvian area in contributing to the expression of a language disorder can be evaluated relative to other areas of abnormality that were documented in language-disordered individuals. Only one autopsy study documented extra-perisylvian effects but in a child with multiple handicaps (Landau et al., 1960). This calls into question the degree to which such findings can be considered correlates of a language disorder. The present study is the first imaging study to examine specific cerebral areas in addition to perisylvian structures. Although other cerebral regions were identified as atypical, no one area was as consistently associated with evidence of a language disorder as was the perisylvian.

The extra-perisylvian findings provide a point of departure between models of acquired and developmental language disorders and their basis in the brain. In acquired language disorders, unilateral damage to the left
perisylvian area is sufficient for the expression of a language disorder. The evidence from this study, and an autopsy report (Galaburda et al., 1985), suggest both widespread and bilateral involvement is typical in cases of developmental language disorder. It is unknown whether the widespread and bilateral damage is a prerequisite for the expression of the language disorder or merely an artifact of the interaction of the causal agent(s) with the course of brain development. It is possible that the widespread and bilateral involvement is one factor limiting the brain's ability to compensate and overcome the structural limitations of the left perisylvian area, thus explaining the persistent nature of the disorder in many of the subjects studied here and elsewhere (e.g. Aram, Ekleman, & Nation, 1984; Aram & Nation, 1980; Griffiths, 1969; Hall & Tomblin, 1978).

The widespread and bilateral involvement provides a potential neuroanatomical explanation for the nonlinguistic deficits documented in groups of specifically language-impaired children (Johnston & Smith, 1989; Johnston & Weismer, 1983; Kamhi, 1981; Kamhi, Catts, Koenig, & Lewis, 1984; Kamhi, Catts, Mauer, Apel, & Gentry, 1988; Nelson, Kamhi, & Apel, 1987; Savich, 1984). Although nonverbal skills have been addressed from a variety of theoretical
frameworks, certain similarities recur across studies in the types of tasks that specifically language-impaired children perform poorly. These tend to be tasks that involve spatial imagery and rotation. Others have interpreted the association of both language and these types of nonverbal deficits as reflecting a generalized deficit in symbolic manipulation (Kamhi, 1981). In light of the current neuroanatomical findings, the behavioral constellation of verbal and select nonverbal deficits co-occur in SLI children because these children have bilateral brain involvement. From this perspective, it is not surprising that language deficits are associated with the type of nonverbal deficits frequently associated with right hemisphere damage.
APPENDIX A

Standardized Test Battery

Nonverbal measures:

Performance criterion:

All nonverbal scales appropriate to the child's age were administered. To be considered for this study, probands had to score above -1.5 SD according to the test's normative data. No exclusion criterion was used for siblings on this measure.

Kaufman Assessment Battery for Children (K-ABC) (Kaufman & Kaufman, 1983)

Test description:

The K-ABC consists of a series of subtests that require nonverbal responses. The subtests were designed to tap skills that require "simultaneous" and "sequential" processing skills. The subtests include Triangles, which requires the child to construct a pictured figure using blue and yellow triangles. Matrix Analogies requires the child to select a geometric figure that corresponds to a given figure in the same way as a previously presented pair are related. Spatial Memory requires a child to remember the locations of pictured items. Hand Movements requires the child to repeat a series of hand movements demonstrated by the examiner. Photo Series requires the child to order a series of photographs to show a sequence of events.

Vineland Social Maturity Scale (Vineland) (Sparrow, Balla, & Cicchetti, 1984)

Test description:

The Vineland is a parent-interview scale that samples daily living and social skills to assess the child's typical behaviors. Parents of children ages 5;11 and below are also surveyed concerning their child's motor skills.
Language measures

Morpho-syntactic:

Performance criterion:

To qualify as a proband, a boy had to score at or below -1.64 SD below the normative sample mean on one or more of the morpho-syntactic tests. No criterion was set for siblings.

Clinical Evaluation of Language Functioning-Revised (CELF-R) (Semmel, Wiig, & Secord, 1987)

Six subtests contribute to computation of an overall language level for children 8;0 and above. Oral Directions taps the child's ability to follow directions of varying length and complexity. Word Classes requires the child to identify which two of four words go together semantically. Semantic Relations requires the child to identify spatial, temporal, and attributional relations. Formulated Sentences requires the child to make up a sentence using a given word. Recalling Sentences requires the child to repeat verbatim sentences spoken by the examiner. Sentence Assembly requires the child to make two sentences from a group of written words.

Subtests of the CELF-R that are known to discriminate between language-impaired and language-normal children (Semmel, Wiig, & Secord, 1987) were administered to children ages 8;0 and above. These include Oral Directions, Semantic Relations, Recalling Sentences, and Sentence Assembly. Additional subtests that contribute to the computation of an overall language level were also administered to most children.

Illinois Test of Psycholinguistic Abilities--Grammatical Closure subtest (ITPA-GC) (Kirk, McCarthy, & Kirk, 1968)

In giving the ITPA-GC, the examiner prompts the child to say words that contain grammatical morphemes using a sentence closure task.

Northwestern Syntax Screening Test--Expressive subtest (NSST-E) (Lee, 1969)
The NSST-E requires the child first to listen to two sentences that correspond to two pictures. Then, the child is asked to repeat the sentences verbatim.

Test of Auditory Comprehension of Language-Revised (TACL-R) (Carrow-Woodfolk, 1985)

The TACL-R requires the child to point to a picture that corresponds to an orally presented word or sentence. The TACL-R has three subtests: Word Classes and Relations, Grammatical Morphemes, and Elaborated Sentences.

Token Test for Children (Token) (DiSimoni, 1978)

The Token has five subtests that require the child to touch or manipulate colored shapes in response to oral directions. The first four subtests increase the length of directions while the fifth increases the linguistic complexity of the directions.

Vocabulary:

Performance criterion: None used.

Peabody Picture Vocabulary Test-Revised (PPVT-R) (Dunn & Dunn, 1981)

The PPVT-R requires the child to point to one of four pictures that corresponds to a word said by the examiner.

Expressive One Word Picture Vocabulary Test (EOWPVT) (Gardner, 1979)

The EOWPVT requires the child to name a word when shown its picture.

Articulation:

Performance criterion: None used.

Templin-Darley Test of Articulation (Templin-Darley) (Templin & Darley, 1968)

The Templin-Darley samples the child's single word articulation skills through picture naming. Normative data
is available for children ages 8 and below.

**Spontaneous Language Analysis**

**Performance criterion:** None used.

**Developmental Sentence Scoring (DSS) (Lee, 1974)**

The DSS analyses 50 consecutive sentences (utterances that have a subject and predicate) from a spontaneous speech sample elicited by a clinician. A DSS was used on language samples from children ages 7;11 and younger.
Child Language Laboratory
MRI and Language Impairment in Children
Case History

CHILD'S FORM

Date: ________________________ 

Person completing this form: ________________________________

Relation to child: ______________________________

IDENTIFYING INFORMATION:

Child's name: ________________________________

Address: _____________________________________

Phone: __________________________

Family: Father

years of education: __________________________

Occupation: ____________________

Mother

years of education: __________________________

Occupation: ____________________

Children: Names | Sex | Age | Grade

| __________________________ | ______ | ______ | ______ |
| __________________________ | ______ | ______ | ______ |
| __________________________ | ______ | ______ | ______ |

Are there any other persons living in your household

Names: __________________________ Relationship to family: __________________

Child's doctor: __________________________

phone: __________________________

Is your child currently receiving speech-language therapy: ______

For how long: __________________________

Child's Speech-Language Therapist: __________________________

Clinic name: __________________________

phone: __________________________

STATEMENT OF THE PROBLEM:

Describe in your own words what problem your child is having with speech,

_____________________________________________________________________

_____________________________________________________________________

When was the problem first noticed: __________________________

Who first noticed the problem: __________________________
What changes in your child's language or speech have you noticed since then:

______________________________________________________________

Do you have any thoughts on the cause of the problem? Please describe:

______________________________________________________________

What have you done to try to help your child's speech:

______________________________________________________________

Has it helped:

______________________________________________________________

Is your child aware of having difficulty with speech or language:

______________________________________________________________

If so, how does he react:

______________________________________________________________

Do any relatives have problems with speech or language:

If so, relation to child: ____________________________ age ______

______________________________________________________________

Do any relatives stutter or stammer:

If so, relation to child: ____________________________ age ______

______________________________________________________________

Do any relatives receive special services in school:

______________________________________________________________

Do any relatives have a developmental disorder (e.g. Dyslexia, Autism, Down syndrome, attention deficit disorder, hyperactivity, learning disabilities or others)

If so, relation to child: ____________________________ type of developmental disorder

______________________________________________________________

What hand does your child prefer to use: right________ left______ either hand______

Are any of the child's family members left handed ______

If so, how many family members ______

Are any of the child's relatives left handed ______

If so, how many relatives ______

SPEECH, LANGUAGE AND HEARING DEVELOPMENT

Did the child make babbling or cooing sounds during the first 6 months of life

______________________________________________________________

At what age did the child say his first word:

______________________________________________________________
What was his first words: ____________________________________________

Did the child keep adding words once he started to talk: ______________

At what age did he start using 2 and 3 word sentences: ______________

Examples: ____________________________________________________________

Did speech learning ever seem to stop for a period of time: ____________

If so, when ____________________________

Do you have any thoughts on the possible cause: ______________________

Does your child talk frequently _______, occasionally _______, never _______.

Does he prefer to talk ________, gesture ________, talk and gesture ________.

Does he frequently use sounds only______, single words______,

2 word sentences______, 3 word sentences______,

more than 3 word sentences______. Examples: __________________________

Can he tell a simple story: ____________________________________________

Does your child make sounds incorrectly: _______ If so, which ones_____

How well is he understood by his parents: _______________________________

by sisters and brothers_________________________________________________

by relatives and strangers_____________________________________________

Will he get common objects when he's asked to: ________________________

Does he ever have trouble remembering what you have told him: __________

If so, when does this happen: ________________________________

Does your child use any books or records: ______________________________

Does he enjoy being read to: ____________________________________________

Describe any recent changes in your child’s speech ______________________

______________________________________________________________

BIRTH HISTORY:

This is our biological______, foster______, adopted______ child.

How many pregnancies has the mother had______, has the mother had any miscarriages______, stillbirths______, abortions______

If so, which pregnancies______,

which pregnancy was this child______,

Mother's age at the time of the child's birth: __________.

Where was the child born (town)______________________________.

Where was the mother born (town)______________________________.

Where was the father born (town)______________________________.

Were there any medical problems before this pregnancy______,

during the pregnancy______,

If so, what________________________________________________________________
Did the mother have any of the following during the pregnancy:  
German measles  Toxemia  Anemia  Accidents/injuries  Kidney Infections  

Did the mother take any prescription or nonprescription drugs (including alcohol) during the pregnancy:  
If so what  

Did the mother smoke during pregnancy  
If so, how many cigarettes per day  

Did the father smoke during the pregnancy  
If so, how many cigarettes per day  

Does either parent or any member of the household currently smoke  
If so who  how much  

Was the mother given drugs during delivery  
What was the child's AFGAR score (if known)  

Any birth injuries  
Was the child a blue baby  
Did the child require oxygen  
Was the child an Rh baby  
Did the child receive any special medications or treatment at birth  
If so, what  

How long were the mother and child in the hospital  
Any comments about the pregnancy or birth  

EDUCATIONAL HISTORY:  
Did or does your child attend day care  Nursery school  Kindergarten  grade school  
For what subjects is he an average student  above average  below average  
Does he receive special help in school  describe  

What is your impression of your child's learning ability  

Has your child received any special education, psychological or hearing services at school  If so, describe (include child's age at the time  

What things does the child do particularly well  

Does he have any special interests or talents  

Describe his personality briefly  

**MEDICAL HISTORY**

Please check if your child, any members of his immediate family (parents, brothers, or sisters) or any other relatives (grandparents, aunts, uncles, cousins) have had any of the following. Only report on blood relatives.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Child</th>
<th>Family</th>
<th>Relatives</th>
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</thead>
<tbody>
<tr>
<td>Allergies</td>
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<tr>
<td>Asthma</td>
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<td>Blood disease</td>
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<td>Bowel disorders</td>
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<td>Chronic colds</td>
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<td>Celiac disease</td>
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<td>Convulsions</td>
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<td>Dermatomyositis</td>
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<td>Diabetes Mellitus</td>
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<td>Diphtheria</td>
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<td>Ear infections</td>
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<td>Encephalitis</td>
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<td>Chronic Headaches</td>
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<td>Head injuries</td>
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<td>High fevers</td>
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<tr>
<td>Whooping cough</td>
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</table>

**DEVELOPMENTAL HISTORY**

Did your child have feeding problems _____ describe____________________

Did your child have sleeping problems _____ describe____________________

When did your child first:
- sit unsupported______
- reach for an object______
- walk unaided______
- bladder trained______
- night trained______
- crawl______
- stand______
- run______
- bowel trained______
Has your child had middle ear infections?
   At what age was the first one?
   Did they occur frequently? Describe the frequency.

Has he been seen by a doctor concerning these infections?
   Did he ever have tubes inserted into his ear drums?
   For how long?

Are the ear infections still occurring? How frequently?

If not, at what age did they stop?

Did the child ever have seizures or convulsions?
   If so, when?
   How frequently?
   Was medical attention sought?
   What was the outcome?

Describe any other illnesses, accidents, injuries, operations and hospitalizations the child has had (include the age of the child at the time).

Is the child now under any medical treatment or taking any medication?
   If so, describe:

Is the child's health good?

Are there any twins in the family or among relatives?
   Relation to child:

Are the twins on the mother's or father's side of the family?
Are the twins identical or fraternal?
**Child Language Laboratory**

**MRI and Language Impairment in Children**

**Case History**

**ADULT FORM**

Date: ________________________ 

**IDENTIFYING INFORMATION:**

Your name: ____________________________________

Address: ______________________________________

Phone: ________________________________

Your occupation: ______________________________

Your Family:

Father: years of education: ______________________

Occupation: ________________________________

Mother: years of education: ______________________

Occupation: ________________________________

Number of brothers: Number of sisters: Number of half-brothers: Number of half-sisters:

<table>
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<tr>
<th>Children</th>
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</tr>
</tbody>
</table>

Are there any other persons living in your household

Names: ____________________________________________

Relationship to family: ____________________________________________

Your doctor: ________________________________

phone: ________________________________

Do you have any metal in your body (e.g. surgical clips, pins) ______

Are you currently pregnant ______

Do you have a serious problem with claustrophobia ______

**SPEECH, LANGUAGE AND HEARING DEVELOPMENT**

Were you a late talker?    yes no  don't know

if yes, when did you begin to use words ________________________________

Did you have any difficulty with speech or language as a child?

 yes no  don't know

if yes, describe ________________________________

Did you have any difficulty pronouncing certain sounds?

 yes no  don't know

if yes, describe ________________________________
Did you stutter?  ____ yes  ____ no  ____ don't know

If yes, until what age __________________________

Did you have any trouble learning to read?  ____ yes  ____ no

If yes, describe __________________________________________________________

Do you enjoy reading today?  ____ yes  ____ no  ____ I don't read much

Did you receive any special services in school?  ____ yes  ____ no

If yes, describe __________________________________________________________

Did you as a child have any difficulties similar to those you see in your child?  ____ yes  ____ no

If yes, describe __________________________________________________________

Do you have any sisters, brothers, nieces or nephews with similar speech or language difficulties?  ____ yes  ____ no

If yes, relation to you ____________________________________________

Do any relatives have problems with speech or language:______________

If so, relation to you: ________________________________ age____

__________________________________________________________

Do any relatives stutter or stammer:______________

If so, relation to you: ________________________________ age____

__________________________________________________________

Do any relatives receive special services in school:______________

If so, relation to you: ________________________________

__________________________________________________________

Do any relatives have a developmental disorder (e.g. Dyslexia, Autism, Down syndrome, attention deficit disorder, hyperactivity, learning disabilities or others)

If so, relation to child type of developmental disorder

________________________

________________________

________________________
BIRTH HISTORY:
Were you adopted?    yes    no
Were any of your relatives adopted?    yes    no
If yes, relation to you ____________________________________________

How many pregnancies did your mother have______
Did your mother have any miscarriages______, stillbirths______
If so, which pregnancies______
Which pregnancy were you______
Your mother's age at the time of your birth:______

Where were you born (town)____________________
Where was your mother born (town)____________________
Where was your father born (town)____________________

Were there any medical problems when your mother was pregnant with you?
    yes    no    don't know
If so, what__________________________________________

Was your mother under unusual stress while pregnant with you______

Did your mother take any prescription or nonprescription drugs (including alcohol) during the pregnancy?    yes    no    don't know
If so what____________________________________________________________________

Did your mother smoke during pregnancy______
    If so, how many cigarettes per day______
Did your father smoke during the pregnancy______
    If so, how many cigarettes per day______

Were you delivered ______ full term ______ premature(_______ months)
Was delivery ______ normal ______ cesarian ______ breach ______ don't know
Any birth injuries______
Were there any medical concerns at birth ______ yes ______ no ______ don't know
If so, what__________________________________________

Any comments about the pregnancy or birth______________________________________

DEVELOPMENTAL HISTORY:
Did you have any difficulty with

    ______ sleeping    ______ standing    ______ toilet training
    ______ eating    ______ walking

What hand do you prefer to use: right____ left____ either hand____

Are any of your family members left handed______
    If so, how many family members______

Are any of your relatives left handed______
    If so, how many relatives______

Are there any twins in the family or among relatives______
    relation to you ________________________________

Are the twins in ____your family ____mother's side or ____father's side of
    the family
Are the twins ______ identical or ______ fraternal.
EDUCATIONAL HISTORY:
I completed grade school, ____ highschool, ____ technical school, ____ college
My last degree obtained was ________________________________.
For what subjects were you an average student?
above average ____________________________________________
below average ____________________________________________
My favorite subject was ________________________________
My least favorite subject was ________________________________
Did you enjoy academics? ____ If no, explain ________________________________
Do you have any further comments on your school experiences? ________________

What do you do particularly well today ____________________________________________
Do you have any special interests or talents ____________________________________________

Did you have middle ear infections as a child ____ yes ____ no ____ don't know
Did any of your family or relatives have middle ear infections? ____ yes ____ no ____ don't know

Have you ever have seizures or convulsions ____ yes ____ no
If so, when ____________________________________________
how frequently ____________________________________________
was medical attention sought ____________________________________________
what was the outcome ____________________________________________

Describe any other illnesses, accidents, injuries, operations and hospitalizations you have had (include the age at the time), ____________________________________________

Are you now under any medical treatment or taking any medication ______
If so, describe: ____________________________________________

Have you ever had any of the following:
___ stroke ___ head trauma ___ epilepsy
MEDICAL HISTORY:

Please check if you, any members of your immediate family (parents, brothers, sisters, or children) or any other relatives (grandparents, aunts, uncles, cousins) have had any of the following. Only report on blood relatives.

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<thead>
<tr>
<th>Condition</th>
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<tbody>
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<tr>
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<td>Blood disease</td>
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APPENDIX C

Instrumentation

- JVC video camera model GX-HBPC9(U)
- Truevision TARGA MB video digitizing board
- IBM PS2/30 model 8530-E21
- Magnavox RGB Display 80 model CHB762 (for image display)
- IBM mouse
- Light box with 12 inch, 32 watt circular fluorescent bulb
APPENDIX D

MRI Measurement Protocols

I. Calibration.

A. Height and level of two lightboxes were measured and verified as identical within the limits of measurement. Lightboxes were used interchangeably.

B. Two carpenters levels, placed on the camera and lightbox, were used to verify that the camera tilt was level with the lightbox (and counter-top) tilt.

C. A calibration check was performed daily.
   1. The plane of the camera and light-box were judged to be parallel by reading levels placed on each.
   2. A calibration figure of 300 millimeters squared was placed at a random angle on the lightbox and measured. This was repeated twice so that three calibration measures were taken a day.

II. General measurement procedures.

A. All images were place on the center of the screen for measurement.

B. Measures were done from the inferior to the superior slices.

C. Areas in the right hemisphere (left side of MRI) were measured before areas in the left.

D. Homologous areas in the left and right hemisphere were measured in the same sitting.

E. When magnetic inhomogeneities are present, the person measuring adjusted the brightness/contrast to compensate for the differences in pixel intensity across inhomogeneous regions.

F. When measuring perpendicular to the midline, only the medial third of the midline was used as the reference for perpendicular.

G. Partial volumes were excluded from measures.

H. Blood vessels and ventricular volumes were included in measures.

I. When sulci are used as landmarks, the grey-white margin was used to define the end of a sulcus in T2 weighted images. When this margin does not form a narrow, distinct point, the midpoint between two adjacent fiber tracts was used. In cases where a grey-white margin was not visible, the visible end of the sulcus was used.

J. Persons measuring scans were trained on MRI scans of subjects not used in this study. The measurement rules
and anatomy books (primarily DeArmond, Fusco, & Dewey, 1976 and Takayoshi & Asao, 1978) were available to assist in identifying anatomical landmarks.

III. Hemispheric measures.

A. Measures started from the anterior pole of the hemisphere and follow the cortical edge.

B. On slices where the hemispheres are connected, a straight line connected the anterior and posterior junctures of the hemispheres.

C. The brainstem was excluded from hemisphere measures.

D. In a small number of scans where full cerebral volumes were not included on axial scans, the coronal view was used to obtain hemispheric volumes. Data, presented below, from individuals who had both axial and coronal scans that included the full cerebral volume indicated no difference in the hemisphere volumes obtained using either view, and that volumes obtained from either view were highly correlated (r=.98 right hemisphere; r=.94 left hemisphere).

IV. The Frontal Lobe

A. Superior Frontal Gyrus area (SFG).

1. The SFG began on the first slice in which the orbital gyrus is no longer visible.
2. It started at the sulcus posterior to the medial branch of the SFG.
3. The starting point was connected, with a straight line, to the anterior-lateral edge of the head of the caudate nucleus. If this point was not visible, the anterior-lateral edge of the lateral ventricles was used.
4. This point was connected, with a straight line, to the superior frontal sulcus.
5. The measure then followed the cortical edge to the starting point.
6. The measure ended on the last slice in which the body of the caudate nucleus was visible, below the area of the centrum semiovale.

B. Middle Frontal Gyrus area (MFG).

1. The MFG began on the first slice in which the orbital gyrus was no longer visible.
2. It started at the edge of the cortex at the juncture of the SFG and MFG.
3. From there it followed the superior frontal sulcus to the grey-white margin.
4. This point was connected, with a straight line, to the anterior-lateral edge of the caudate nucleus (see also B-3 above).
5. This point was connected, with a straight line, to the grey-white margin of the inferior frontal sulcus.
6. The measure followed the sulcus to the cortical edge.
7. The cortical edge was traced to the starting point.
8. The measure ended on the last slice in which the body of the caudate nucleus is visible, below the area of the centrum semiovale.

C. Inferior Frontal Gyrus area (IFG).

1. The IFG began on the first slice in which the orbital gyrus was no longer visible.
2. It started at the cortical edge at the juncture of the MFG and IFG.
3. From this point, it followed the inferior frontal sulcus to the grey-white margin.
4. This point was connected, with a straight line, to the anterior-lateral edge of the head of the caudate nucleus (see also B-3 above).
5. This point was connected, with a straight line, to the juncture of the IFG and the pars triangularis.
6. The cortical edge was traced to the starting point.
7. The measures ended when the IFG was no longer visible.

D. Anterior Cingulate area.

1. The anterior cingulate area began on the first slice in which the genu of the corpus callosum was visible.
2. It started at exterior edge of the cingulate sulcus, defined as the first sulcus anterior to the corpus callosum.
3. From this point, it followed the sulcus interiorly to the grey-white margin.
4. This point was connected, with a straight line, to the most lateral point of the anterior horn of the caudate nucleus.
5. This point was connected, with a straight line, to the juncture of the corpus callosum and cingulate gyrus.
6. The edge of the cortex was traced to the starting point.
7. The measures ended on the most superior slice in which the body of the corpus callosum is visible.

V. Perisylvian area (PSA).

A. The PSA began on the first slice on which a sylvian fissure was seen, typically just superior to the middle cerebral arteries.
B. The most medial-posterior pixel of grey matter at the end of the sylvian fissure was located. When multiple Hescl's gyri were visible, the sylvian was defined as posterior to the first Hescl's gyrus (c.f. Witleson & Pallie, 1971).
C. This point was connected, with a line drawn perpendicular to the midline, to the cortical edge.
D. The cortical edge was followed anteriorly to the medial-most edge of the temporal poles or to the posterior margin of the IFG.
E. This point was connected, with a straight line, to the starting point.
F. The measures ended on the last slice in which the insula was visible.

VI. Temporal Lobe.

A. Middle Temporal Gyrus area (MTG).
1. The MTG began on the most inferior slice on which some portion of the occipital pole and gyrus rectus was visible.
2. The most medial-posterior pixel of grey matter corresponding to the most anterior and lateral lobule of the temporal lobe was located.
3. This point was connected, with a line drawn perpendicular to the midline, to the cortical edge.
4. The cortical edge was followed posteriorly to the temporal-occipital sulcus, defined as anterior to the second girl convolution from the occipital pole (this gyrus may have two visible branches).
5. This point was connected, with a straight line, to the starting point.
6. The MTG ended at the level of the perisylvian area.
C. Superior Temporal Gyrus area (STG).

1. The STG began on the second slice of the PSA.
2. The most medial-posterior pixel of grey mater at the end of the sylvian fissure was located. When multiple Heschl's gyri are visible, the sylvian was defined as posterior to the first Heschl's gyrus.
3. This point was connected, with a line drawn perpendicular to the midline, to the cortical edge.
4. The measure followed the cortical edge posteriorly to the temporal-occipital sulcus, defined as anterior to the second girl convolution from the occipital pole (this gyrus may have two visible branches).
5. This point was connected, with a straight line, to the starting point.
6. The STG ended on the slice below the level on which the splenium of the corpus callosum is visible.

VI. Occipital area (Occip.).

A. The Occip. began on first slice on which occipital poles are visible.
B. Measurement started at the juncture of the temporal and occipital lobes (see V. B-4 above).
C. This point was connected with the anterior juncture of the cerebellum and cerebrum.
D. The measure traced the edge of the cortex, around the occipital poles, to the starting point.
E. The Occip ended on the slice below the level on which the splenium of the corpus callosum was visible.

VII. Parietal Lobe

A. Supramarginal/angular gyrus area (SMG/ANG).

1. The SMG/ANG began on the first slice in which the splenium of the corpus callosum is seen completely bridging the hemispheres.
2. Measurement started at the most medial-posterior margin of the sylvian fissure (see also V. B-4 above).
3. This point was connected, with a line drawn perpendicular to the midline, to the cortical edge.
4. The measure followed the cortical edge posteriorly to the interparietal sulcus, defined as anterior to the second girl convolution from the occipital pole (these gyri may have two visible branches).
5. This point was connected, with a straight line, to the starting point.
6. The SMG/ANG ended on the last slice below the centrum semiovale.
Differences between hemispheric measures taken from brains cut in coronal and axial sections.

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<th>Subject</th>
<th>Coronals</th>
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Distribution of Differences between Coronals and Axials Measures

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Inter-operator differences in axial hemispheric measures.

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<th>Axials-2</th>
<th>Differences</th>
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<td>381.13</td>
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<td>4</td>
<td>334.27</td>
<td>332.30</td>
<td>344.82</td>
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<td>5</td>
<td>386.37</td>
<td>376.86</td>
<td>387.77</td>
</tr>
<tr>
<td>6</td>
<td>398.44</td>
<td>394.17</td>
<td>391.91</td>
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<tr>
<td>7</td>
<td>294.80</td>
<td>295.73</td>
<td>292.49</td>
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<tr>
<td>8</td>
<td>388.97</td>
<td>386.03</td>
<td>374.48</td>
</tr>
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</table>

Distribution of Inter-operator Differences

-20
---0---20
+++++++-----------------------------

Correlated t test for difference between inter-operator differences in axial measures and coronal-axial differences.

right hemisphere differences t= 0.79, df=7, p > .10
left hemisphere differences t=0.45, df=7, p > .10

Pearson product moment correlation for axial and coronal hemisphere measures.

right hemisphere r = 0.98, df = 6, p < .01
left hemisphere r = 0.94, df = 6, p < .01
APPENDIX E

A Pilot Study of Regional Brain Measures

Method

Subjects

Three boys who were identified as specifically language impaired with deficits in the comprehension or use of grammatical morphemes served as subjects for this pilot study. These subjects were previously described in a separate paper (Plante, Swisher, Vance, and Rapcsak, 1990). None served as subjects in this dissertation study.

Scans from these three boys were compared with comparison scans from 10 normal male volunteers. Comparison scans met the same selection criteria detailed in the methods section of this dissertation.

Procedures

Measurement protocols for ten regions of the brain were developed on the normal volunteers. Regional measures were developed with consideration for differences in their time of development (cf. Chi, Dooling, & Gilles, 1977). These protocols are detailed in Appendix D. Measurement protocols used anatomical landmarks that could be clearly identified on all brains. This accomplished several goals. First, it increased the likelihood that the protocol could be followed reliably across subjects. It also insured measurements would be more sensitive to individual variations in brain configuration than more arbitrary divisions of the brain (e.g. grids). Regional brain volumes were converted into proportions of the total brain volume to eliminate the effects of brain size on the measurements.

A protocol for any given area was considered reliable when intra-operator reliable measures were obtained on all control scans used in this pilot effort. Measures were considered reliable when volumes for all control scans obtained on two sessions correlated at or above \( r = .83 \) (70% shared variance) using a Pearson's product-moment correlation. Reliability figures for measurements on both subject and control scans ranged between .87 and .99.

Regions above the level of the centrum semiovale were not measured. This was partially due to the limitations of using axial scans. Regions towards the top of the brain were affected by partial volume effects due to the marked curvature of the brain on the more superior slices. This effect limited the extent to which anatomical landmarks
could be reliably identified. Similar problems interfered with measurement of gyrus rectus, therefore it was excluded from the group of measures.

Results

The results of the pilot study are given in the table below. A z-score was calculated for each regional brain volume. This facilitated a comparison of the subject scans and comparison scans. Z-scores beyond +/-1.30 ($p < .20$) in any subject were considered to indicate a measure of potential interest for additional study. The following measures met this criterion: inferior frontal area, middle frontal area, superior frontal area, superior temporal area, middle temporal area, perisylvian area, supramarginal area, occipital lobe. Several measures, the inferior frontal area, and the superior and middle temporal areas were significantly ($z > +/-1.96; p < .05$) different from normal in at least one subject. The earliest developing area, the anterior cingulate area, was not markedly different in the SLI boys than in the comparison group. Measures for this area will not be reported for dissertation subjects.
Table
Proportional volumes of brain regions from three SLI-GI boys.

<table>
<thead>
<tr>
<th>Brain region</th>
<th>Adam volume</th>
<th>Brian volume</th>
<th>Cory volume</th>
<th>controls mean</th>
<th>controls SD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>z</td>
<td>z</td>
<td>z</td>
<td>volume</td>
<td></td>
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<tr>
<td>Rt. Cingulate</td>
<td>0.51</td>
<td>0.47</td>
<td>0.48</td>
<td>0.48</td>
<td>0.16</td>
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<tr>
<td>Lf. Cingulate</td>
<td>0.57</td>
<td>0.47</td>
<td>0.51</td>
<td>0.50</td>
<td>0.17</td>
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<td>0.81</td>
<td>1.10</td>
<td>0.55</td>
<td>0.79</td>
<td>0.14</td>
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<td>Lf. I. Frontal</td>
<td>0.73</td>
<td>1.05</td>
<td>0.81</td>
<td>0.81</td>
<td>0.19</td>
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<td>Rt. M. Frontal</td>
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<td>1.27</td>
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<tr>
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<td>1.32</td>
<td>1.03</td>
<td>1.24</td>
<td>0.26</td>
</tr>
<tr>
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<td>1.88</td>
<td>1.45</td>
<td>1.58</td>
<td>0.34</td>
</tr>
<tr>
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<td>1.92</td>
<td>1.44</td>
<td>1.49</td>
<td>0.33</td>
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<td>1.22</td>
<td>0.25</td>
</tr>
<tr>
<td>Lf. S. Marginal</td>
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<td>1.53</td>
<td>1.18</td>
<td>1.19</td>
<td>0.20</td>
</tr>
<tr>
<td>Rt. Perisylvian</td>
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<td>0.32</td>
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<tr>
<td>Lf. Perisylvian</td>
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<td>1.77</td>
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<td>Rt. Occipital</td>
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<td>3.55</td>
<td>4.04</td>
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<td>1.46</td>
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REFERENCES


