The authors conducted a case-control study to determine whether risk factors for reading disability (RD) differentially affect boys and girls. The study population included all children born between 1976 and 1982 in Olmsted County, Minnesota (n = 5,701). A total of 303 RD cases were identified by using intelligence quotient and achievement test scores collected from school and medical records. After excluding those who met exclusion criteria (n = 869), controls consisted of all children not identified with RD (n = 4,529). The authors examined the association between RD and potential risk factors in boys and girls and confirmed their results in multivariable logistic regression models. Multivariable models indicated that girls of low birth weight were more than twice as likely to be identified as RD (odds ratio (OR) = 2.94, 95% confidence interval (CI): 1.09, 6.25). Girls whose mothers had 12 or fewer years of education were twice as likely to be identified as RD (OR = 2.14, 95% CI: 1.24, 3.72). However, girls whose fathers were aged 35 years or older at the time of birth were less likely to be identified as RD (OR = 0.24, 95% CI: 0.06, 0.92). Only 12 or fewer years of paternal education was associated with increased RD in boys (OR = 2.28, 95% CI: 1.59, 3.27). Boys and girls appear to be differentially susceptible to RD risk factors, suggesting that the biologic processes leading to RD may differ between boys and girls. Am J Epidemiol 2001;154:787–94.
Hence, currently identified risk factors may have different effects on male children compared with female children. For example, male children who are born into families of low socioeconomic status (SES) may be at a particularly high risk for RD, while female children who are born into families with low SES might not be at increased risk for RD.

To address these issues, we performed a post hoc analysis to determine whether potential LD risk factors differentially affect the risk for RD in boys compared with girls in a large, population-based cohort of Olmsted County, Minnesota, schoolchildren.

**MATERIALS AND METHODS**

**Identification of the Rochester birth cohort**

All children (n = 8,548) born between January 1, 1976 and December 31, 1982 to mothers residing in the five Olmsted County, Minnesota, townships (comprising Minnesota Independent School District 535) were identified through computerized birth certificate information obtained from the Minnesota Department of Health, Division of Vital Statistics. To ascertain vital status for each member of the birth cohort during the 1995–1996 school year, resources available from the Rochester Epidemiology Project (20), Independent School District 535, the Reading Center/Dyslexia Institute of Minnesota (RCDIM), and the Minnesota Department of Health were utilized. Current status was assessed for all children (still living in Olmsted County, moved, or deceased). Children who no longer lived in Olmsted County during the 1995–1996 school year (who moved or died before age 5 years) were not included in the final study cohort (n = 2,847).

**Case definition**

All public and private school records, medical records, and records from the RCDIM were accumulated, and a research folder was established for every child remaining in the birth cohort (n = 5,701). We first reviewed the school records of all the children in our birth cohort, looking for any evidence of concern about problems in school learning or school performance. Evidence of a school problem included obvious signs of school difficulty, such as grade retention, presence of a special education learning plan (Chapter I, Title I, or Individualized Education Program), or other supplemental instruction. School records were also carefully examined for subtle signs of learning problems, including any notation indicating that teachers, parents, or anyone else had concerns about the child’s school or learning performance.

Since it was possible that some of the children in our cohort may have had learning difficulties that were never recorded in the school record, we also searched the medical records of all the children for any indication of concern about school problems. The interdisciplinary assessments in the medical system were completed by pediatricians, psychologists, and psychiatrists who specialize in the identification of learning disabilities and behavioral problems. We also searched the records of a local reading center because use of the center by a member of our cohort would imply concern about a learning problem.

These procedures yielded 1,471 children (26 percent of our birth cohort) who had ever used the reading center or who had some indication in their school or medical records of any type of learning problem. We then abstracted all of these children’s individually administered intelligence quotient (IQ) and achievement test scores and applied four ability-achievement discrepancy methods to classify each potential RD candidate. The magnitude of the discrepancy between expected and observed reading performance was determined by four formulas; a regression formula used by the state of Minnesota (21); the regression formula proposed by Shaywitz et al. (22); a standard-score discrepancy-based formula (S. K. Katusic, Mayo Clinic Rochester, Rochester, Minnesota, unpublished manuscript); and a method based solely on low achievement (22–24). Seventeen of the children in the cohort were severely mentally retarded, and these children were excluded from all analyses. If a child was identified as having RD by any of the four formulas and if the RD was not associated with exclusionary criteria described in the Individuals with Disabilities Education Act definition of a learning disability (25), that child was classified as having “pure” RD (table 1).

**Control definition**

All children in the birth cohort who had neither pure RD nor any of the exclusionary criteria described in table 1 made up the control group (n = 4,529).

**Exposure ascertainment**

Demographic characteristics, health of the infant at birth, complications of pregnancy, and characteristics of birth injuries or problems during labor or delivery were abstracted from the birth certificates of all children in the cohort. This included race of the child, mother, and father; estimated gestational age at birth; birth weight; and whether

<table>
<thead>
<tr>
<th>Reason for exclusion</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual problems</td>
<td>6</td>
<td>0.9</td>
</tr>
<tr>
<td>Hearing problems</td>
<td>17</td>
<td>2.4</td>
</tr>
<tr>
<td>Motor impairment</td>
<td>13</td>
<td>1.9</td>
</tr>
<tr>
<td>Mild mental retardation</td>
<td>60</td>
<td>8.6</td>
</tr>
<tr>
<td>Major psychologic disorder</td>
<td>67</td>
<td>9.7</td>
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<tr>
<td>Attention deficit/hyperactivity disorder</td>
<td>180</td>
<td>25.9</td>
</tr>
<tr>
<td>Drug/alcohol abuse</td>
<td>170</td>
<td>24.5</td>
</tr>
<tr>
<td>Abuse/neglect</td>
<td>100</td>
<td>14.4</td>
</tr>
<tr>
<td>Multiple school changes</td>
<td>17</td>
<td>2.5</td>
</tr>
<tr>
<td>Marked absenteeism</td>
<td>68</td>
<td>9.8</td>
</tr>
</tbody>
</table>

* A total of 391 children were excluded from the “pure reading disability” category. Children may have had more than one of the conditions listed.
or not the child was born to a single parent. Specific medical
diagnostic codes were collected for indication of induction
or augmentation of labor, mode of delivery, and any opera-
tive procedures. In addition, the presence of pregnancy-
induced hypertension and gestational diabetes was noted.
Continuous variables (parental age and education level,
child’s birth weight, and gestational age) were categorized
according to cutpoints suggested by the literature.

Statistical analysis

The distribution of potential risk factors in children with
RD was compared with that of risk factors among children
not diagnosed with RD by using chi-square tests. The
strength of the association between each potential risk factor
and RD was estimated by odds ratios and corresponding 95
percent confidence intervals separately for male and female
children. The Breslow-Day test was used to determine
whether odds ratios differed significantly by sex. Multi-
variable logistic regression models containing the factors
significantly associated with RD in univariate analyses were
created separately for boys and girls to determine whether
factors significant in the univariate analyses remained so
after adjustment for other variables. In addition, a multivari-
ate logistic regression model that included all significant
variables from univariate analyses, sex, and significant inter-
action terms from univariate analyses was created, allowing
us to assess the significance of the interaction terms after
adjustment for potential confounders. The Hosmer-
Lemeshow method was used to determine goodness-of-fit of
the logistic models. All calculated p values were two-sided;
p values less than 0.05 were considered to be statistically
significant. Ninety-five percent confidence intervals that
did not include 1.00 were also considered to be statistically
significant.

RESULTS

There were 8,548 children born in the four Olmsted
County, Minnesota, townships between 1976 and 1982.
Approximately one third of this population moved out of
Olmsted County by age 5 years, leaving 5,701 children (2,951
boys and 2,750 girls) as the subjects for this study. These chil-
dren lived in Olmsted County, moved after age 5 years, or
died after age 5. A total of 116 children were identified as hav-
ing RD by the Minnesota school regression formula, 149 by
the Shaywitz regression formula, 212 by the discrepancy for-
mula, and 241 by the low-achievement method. Taken
altogether, 303 (5.3 percent) children were identified as having
RD by any of the four formulas. Since these results were in
the same direction and of approximately the same magnitude,
regardless of the formula used, we report the results on the
children identified as having RD by any of the four formulas.
Our final control group consisted of 4,529 children, after
exclusion of those who met exclusion criteria (n = 869).

Overall, children with RD were significantly more likely
to be male (chi-square p = 0.001) and be born to younger
mothers (chi-square p = 0.05) (table 2). They were also sig-
ificantly more likely to have mothers or fathers with lower
education levels compared with children who did not have
RD (chi-square p = 0.001; table 2).

When risk factors for RD were examined separately for
male and female children, low maternal and low paternal
education was associated with RD in both boys and girls
(table 3). In addition, among female children, low birth
weight and being born a twin were associated with over a
threefold increase in RD. However, paternal age greater than
age 35 years was associated with more than a fourfold
decrease in RD (table 3). Breslow-Day tests indicated that
low birth weight, being born a twin, high paternal age, and
low maternal education differed significantly by sex.

Girls with low birth weight were about 3.5 times more
likely to be diagnosed with RD compared with girls of nor-
mal birth weight (odds ratio (OR) = 3.52, 95 percent confi-
dence interval (CI): 1.81, 6.85). In addition, boys of either
normal or low birth weight were more than twice as likely
to be diagnosed with RD compared with girls of normal
birth weight (OR = 2.81, 95 percent CI: 2.15, 2.68 and
OR = 2.42, 95 percent CI: 1.14, 5.16, respectively) (data
not shown in tables). The odds of RD among girls of low
birth weight, boys of normal birth weight, and boys of low
birth weight did not differ significantly.

In a multivariable model evaluating factors associated
with RD in girls, low birth weight, low maternal education,
and low paternal age remained significantly associated with
RD. However, only low paternal education remained signif-
ically associated with RD in boys (table 4).

DISCUSSION

Our results suggest that male and female children are dif-
ferentially susceptible to risk factors for RD. First, male
children had a 2.5-fold higher risk of RD compared with female
children. Second, female children of low birth weight were at
a 3.5-fold increased risk for RD, but low birth weight did not
increase the risk for RD in male children. Finally, these data
also suggest that sociodemographic factors, such as paternal
age and parental education level, differentially affect the risk
for RD in girls compared with boys. High paternal age
decreased the risk for RD in girls but not in boys. Low mater-
nal education level increased the risk for RD in girls but not
in boys, while low paternal education level increased the risk
for RD in boys but not in girls.

Sex

The reasons for the increased educational and develop-
mental problems experienced by male compared with female
children are unclear, but male children are diagnosed
with a wide range of neurodevelopmental disorders more
often than are female children (26, 27). Shaywitz et al. (7)
have reported that teachers are more likely to refer boys than
girls for special education testing, suggesting that referral
bias accounts for gender differences in LD. Flannery et al.
(5), indicate, however, that when referral bias is excluded
from the study design, boys are at least two times more
likely to have RD compared with girls. In our study, children
were identified as having RD by using information from

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Reading disability</th>
<th>No reading disability</th>
<th>( \chi^2 )</th>
<th>( p ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Child factors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex (male)</td>
<td>215</td>
<td>2,217</td>
<td>49.0</td>
<td>0.001</td>
</tr>
<tr>
<td>Child's race (Caucasian)</td>
<td>297</td>
<td>4,406</td>
<td>97.4</td>
<td>0.52</td>
</tr>
<tr>
<td>Born to a single parent</td>
<td>19</td>
<td>257</td>
<td>5.7</td>
<td>0.67</td>
</tr>
<tr>
<td>Low birth weight (&lt;2,500 g)</td>
<td>19</td>
<td>185</td>
<td>4.1</td>
<td>0.07</td>
</tr>
<tr>
<td>Prematurity (&lt;37 weeks gestation)</td>
<td>3</td>
<td>71</td>
<td>5.6</td>
<td>0.84</td>
</tr>
<tr>
<td>Apgar score (1 minute) &lt;8</td>
<td>14</td>
<td>361</td>
<td>25.1</td>
<td>0.95</td>
</tr>
<tr>
<td>Apgar score (5 minutes) &lt;8</td>
<td>0</td>
<td>47</td>
<td>3.3</td>
<td>0.42*</td>
</tr>
<tr>
<td>Twin</td>
<td>8</td>
<td>88</td>
<td>1.9</td>
<td>0.40</td>
</tr>
<tr>
<td><strong>Parental factors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mother's age (years)</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>15–19</td>
<td>25</td>
<td>262</td>
<td>5.8</td>
<td>0.05</td>
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<td>20–34</td>
<td>268</td>
<td>4,001</td>
<td>88.3</td>
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<tr>
<td>≥35</td>
<td>10</td>
<td>266</td>
<td>5.9</td>
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<tr>
<td>Father's age (years)</td>
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<td></td>
</tr>
<tr>
<td>15–19</td>
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<td>84</td>
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<td>20–34</td>
<td>258</td>
<td>3,656</td>
<td>84.2</td>
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<tr>
<td>≥35</td>
<td>27</td>
<td>600</td>
<td>13.2</td>
<td></td>
</tr>
<tr>
<td>Mother's race (Caucasian)</td>
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<td>4,422</td>
<td>97.8</td>
<td>0.50</td>
</tr>
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<td>Father's race (Caucasian)</td>
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<td>4,299</td>
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<td>0.21</td>
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<tr>
<td>Maternal education &lt;12 years</td>
<td>146</td>
<td>1,560</td>
<td>37.8</td>
<td>0.001</td>
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<tr>
<td>Paternal education &lt;12 years</td>
<td>140</td>
<td>1,268</td>
<td>32.2</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>Pregnancy/labor-delivery characteristics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>&lt;7 prenatal visits</td>
<td>20</td>
<td>439</td>
<td>9.8</td>
<td>0.08</td>
</tr>
<tr>
<td>Pregnancy complications</td>
<td>26</td>
<td>361</td>
<td>8.0</td>
<td>0.70</td>
</tr>
<tr>
<td>Labor/delivery complications</td>
<td>119</td>
<td>1,671</td>
<td>37.0</td>
<td>0.43</td>
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<tr>
<td>Operative procedure required</td>
<td>36</td>
<td>599</td>
<td>13.2</td>
<td>0.50</td>
</tr>
<tr>
<td>Birth injuries</td>
<td>1</td>
<td>38</td>
<td>0.8</td>
<td>0.51*</td>
</tr>
<tr>
<td>Congenital anomalies</td>
<td>2</td>
<td>26</td>
<td>0.6</td>
<td>0.69*</td>
</tr>
<tr>
<td>Intensive-care unit stay</td>
<td>0</td>
<td>27</td>
<td>1.9</td>
<td>0.62*</td>
</tr>
</tbody>
</table>

* Fisher’s exact test p value.

three sources of data—school records, medical records, and records obtained from RCDIM—and applying research criteria for identifying RD. Because we abstracted preexisting data, it is possible that our results could have been biased due to more frequent referral of boys for IQ and achievement testing. However, our data suggest that the boys in our birth cohort were not differentially referred for testing at a higher rate than girls. In our study, 1,951 children were initially identified as having some type of school problem (1,196 boys and 755 girls). While more boys than girls were initially identified as having school problems, 498 girls and 847 boys received IQ and achievement testing (OR = 1.25, 95 percent CI: 0.82, 1.52). Among the children who were not initially identified as having a school problem (1,760 boys and 2,007 girls), 61 girls and 65 boys received IQ and achievement testing (OR = 1.22, 95 percent CI: 0.86, 1.74). Therefore, it seems less likely that referral bias is responsible for the increased rate of RD observed among male children compared with female children in this birth cohort.

Shaywitz et al. (17) have demonstrated that men and women differ in the areas of the brain that are activated during phonologic processing; men tend to activate the left inferior frontal gyrus of the brain, while women activate both the left and the right inferior frontal gyrus. Therefore, girls may be better able to compensate for a deficit in reading compared with boys. Alternatively, Galaburda and Geschwind (6) have suggested that elevated fetal testosterone levels are responsible for the increased number of school problems observed among boys.

**Low birth weight**

Previous studies have indicated that children of low birth weight (less than 2,500 g) are at risk for a wide variety of health and developmental problems (8–13, 16, 28). No previous studies have, however, described a differential effect of birth weight on RD among male and female children. It is unclear why low birth weight would more strongly predispose female children than male children toward RD. Overall, while low birth weight increased the risk for RD in girls, it increased the risk only to about the level typically
TABLE 3. Odds ratios and 95% confidence intervals predicting reading disability in male children and female children, Olmsted County, Minnesota, 1976–1982

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Boys</th>
<th></th>
<th></th>
<th>Girls</th>
<th></th>
<th></th>
<th>Breslow-Day p value*</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Odds ratio</td>
<td>95% CI</td>
<td></td>
<td>Odds ratio</td>
<td>95% CI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Child factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Child's race (Caucasian vs. non-Caucasian)</td>
<td>0.83</td>
<td>0.33, 2.08</td>
<td></td>
<td>0.47</td>
<td>0.06, 3.44</td>
<td>0.61</td>
<td></td>
</tr>
<tr>
<td>Born to a single parent</td>
<td>1.19</td>
<td>0.66, 2.15</td>
<td></td>
<td>1.11</td>
<td>0.48, 2.59</td>
<td>0.90</td>
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</tr>
<tr>
<td>Low birth weight (&lt;2,500 g)</td>
<td>0.86</td>
<td>0.41, 1.80</td>
<td></td>
<td>3.52</td>
<td>1.81, 6.85</td>
<td>0.003</td>
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<tr>
<td>Prematurity (&lt;37 weeks gestation)</td>
<td>1.20</td>
<td>0.27, 5.23</td>
<td></td>
<td>1.12</td>
<td>0.14, 8.70</td>
<td>0.96</td>
<td></td>
</tr>
<tr>
<td>Apgar score (1 minute) &lt;8</td>
<td>1.02</td>
<td>0.49, 2.13</td>
<td></td>
<td>1.06</td>
<td>0.33, 3.37</td>
<td>0.95</td>
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<tr>
<td>Apgar score (5 minutes) &lt;8</td>
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</tr>
<tr>
<td>Twin birth</td>
<td>0.72</td>
<td>0.22, 2.33</td>
<td></td>
<td>3.04</td>
<td>1.17, 7.84</td>
<td>0.05</td>
<td></td>
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<tr>
<td>Parental factors</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Mother's age (referent: 20–34 years)</td>
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<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>15–19</td>
<td>1.32</td>
<td>0.76, 2.31</td>
<td></td>
<td>1.84</td>
<td>0.93, 3.63</td>
<td>0.46</td>
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<tr>
<td>≥35</td>
<td>1.60</td>
<td>0.29, 1.24</td>
<td></td>
<td>0.42</td>
<td>0.10, 1.71</td>
<td>0.65</td>
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<tr>
<td>Father's age (referent: 20–34 years)</td>
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<td></td>
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<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>15–19</td>
<td>0.90</td>
<td>0.32, 2.52</td>
<td></td>
<td>2.41</td>
<td>0.84, 6.90</td>
<td>0.18</td>
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</tr>
<tr>
<td>≥35</td>
<td>0.82</td>
<td>0.52, 1.27</td>
<td></td>
<td>0.23</td>
<td>0.07, 0.74</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>Mother's race (Caucasian vs. non-Caucasian)</td>
<td>0.97</td>
<td>0.59, 1.60</td>
<td></td>
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<td></td>
<td></td>
<td>0.17</td>
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<td>Father's race (Caucasian vs. non-Caucasian)</td>
<td>0.44</td>
<td>0.15, 1.29</td>
<td></td>
<td>0.83</td>
<td>0.29, 2.38</td>
<td>0.75</td>
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<tr>
<td>Maternal education ≤12 years</td>
<td>1.52</td>
<td>1.14, 2.04</td>
<td></td>
<td>2.68</td>
<td>1.70, 4.22</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>Paternal education ≤12 years</td>
<td>2.25</td>
<td>1.67, 3.04</td>
<td></td>
<td>2.33</td>
<td>1.49, 3.64</td>
<td>0.90</td>
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<tr>
<td>Pregnancy characteristics</td>
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<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;7 prenatal visits</td>
<td>0.61</td>
<td>0.34, 1.09</td>
<td></td>
<td>0.79</td>
<td>0.36, 1.74</td>
<td>0.60</td>
<td></td>
</tr>
<tr>
<td>Pregnancy complications</td>
<td>1.06</td>
<td>0.65, 1.74</td>
<td></td>
<td>1.05</td>
<td>0.48, 2.32</td>
<td>0.99</td>
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<tr>
<td>Labor/delivery complications</td>
<td>0.90</td>
<td>0.68, 1.20</td>
<td></td>
<td>0.96</td>
<td>0.62, 1.49</td>
<td>0.80</td>
<td></td>
</tr>
<tr>
<td>Operative procedure required</td>
<td>0.74</td>
<td>0.47, 1.17</td>
<td></td>
<td>1.25</td>
<td>0.70, 2.25</td>
<td>0.16</td>
<td></td>
</tr>
<tr>
<td>Birth injuries</td>
<td>0.59</td>
<td>0.07, 3.65</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.57</td>
</tr>
<tr>
<td>Congenital anomalies</td>
<td>1.59</td>
<td>0.36, 7.10</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.38</td>
</tr>
<tr>
<td>Intensive-care unit stay</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Breslow-Day p values less than 0.05 indicate that odds ratios differ significantly between boys and girls.
† CI, confidence interval.

experienced by male children of normal birth weight. Therefore, the effect of low birth weight may not be as noticeable in boys because boys already have a higher baseline rate of RD.

Altogether, 249 children in our cohort met the criteria for low birth weight (weight <2,500 g). We examined this group by sex to determine whether boys of low birth weight were more likely to experience other learning problems that might exclude them from the pure RD classification by using the Fisher’s exact test. We found that boys of low birth weight were more likely to have attention deficit hyperactivity disorder compared with girls (11.5 vs. 0.9 percent; p < 0.01), but did not significantly differ from girls in any other category. In addition, our results remained the same regardless of whether or not these children were included in our analyses (data not shown). Therefore, the observed sex differences do not appear to be due to differential exclusion of boys from the pure RD classification.

Sociodemographic variables

Our data also suggest that sociodemographic factors predispose girls and boys to RD. For example, we found that low parental education level was associated with an overall increased risk of LD for both boys and girls. Parental education is frequently used as a marker for SES (29), and low SES has frequently been demonstrated to be an important risk factor for later school difficulties (11, 13, 30, 31). It is not clear, however, how SES exerts its effect on the development of RD. Low SES may be a marker for parental educational difficulties (i.e., suggesting a genetic component in RD development), or it may be a marker for specific environmental factors.

Overall, while low maternal and paternal education increased the risk for RD in both boys and girls, our data suggest that low parental education affected male and female children differentially. In multivariable models, low
maternal education level was a significant risk factor for RD in girls, but not in boys, while low paternal education was a significant risk factor for RD in boys, but not in girls. A significant interaction was observed only between sex and maternal education. Previous studies have suggested that maternal education tends to predict a daughter’s educational attainment (32, 33). In addition, having female teachers as role models also predicts increased educational attainment in girls, but not in boys (34). These studies suggest that socialization patterns for girls differ from those of boys and that appropriate female role models may improve girls’ academic achievement. By analogy, appropriate parental male role models may improve boys’ academic achievement. These factors may also be important in our study population and may explain why, in our birth cohort, low maternal education is a risk factor for RD in girls, while low paternal education is a risk factor for RD in boys.

Higher paternal age (35 years or older) was associated with decreased RD in girls but not in boys. Older paternal age was modestly correlated with higher paternal education level (correlation coefficient = 0.28; p = 0.0001). It is possible that older, more educated fathers may make more of an effort to participate in their daughters’ education compared with younger, less educated fathers.

### Strengths and weaknesses

We thoroughly reviewed all medical and school records and independently determined whether or not a child had RD. This process allowed us to minimize some of the referral bias that may be present in studies in which the samples were derived from teacher or parent referral. In addition, our study had a substantially larger sample size than did most previous studies of LD, allowing us to consider interactions of potential risk factors with child’s sex.

A potential limitation of our study is that 33 percent of the original birth cohort migrated from Olmsted County by age 5 years. If the children who migrated from Olmsted County differed significantly in birth characteristics and/or in incidence of RD, our study results may be biased. Katusic et al. (35) addressed this issue and demonstrated that few differences in birth characteristics existed between migrant and nonmigrant children. Of the observed differences, none is likely to be of concern for evaluating potential RD risk factors.

Because we examined 20 potential RD risk factors, it is also possible that an alpha level of 0.05 was not sufficiently stringent for defining statistical significance. Thus, to protect against type I error, a p value of 0.003 or less might have been more appropriate (36). However, most of our reported associations (low paternal education in boys and low maternal education and low birth weight in girls) achieved this level of significance in univariate models (table 2), so we believe it is unlikely that our results were due to type I error.

We used birth certificate data as our source for potential risk factor information. Previous studies have demonstrated that much of the information captured on birth certificates is valid and reliable, particularly that on birth weight and maternal and paternal demographic characteristics (37–39). Other data, such as pregnancy, labor, and delivery complications, tend to be underreported on birth certificates (37–40). Therefore, it is possible that some complications among our study population were missed. If the children who were reading disabled had more complications of pregnancy, labor, and delivery than did children who were not reading disabled, we will underestimate the association between these complications and RD. If the children who were reading disabled had fewer pregnancy, labor, and delivery complications, this might explain why we did not see associations (low paternal education in boys and low maternal education in girls) achieved this level of significance in univariate models (table 2).
delivery complications than children who were not reading disabled, we will overestimate the association between these complications and RD. However, we have no reason to believe that the quality of the birth certificate data varied by outcome or by sex. Further studies are needed to examine the association of other potential risk factors not included on birth certificates with RD. These include maternal smoking, use of drugs or alcohol, hypertension, other maternal health conditions, use of medications, pre- and perinatal child illnesses, and intrauterine growth retardation.

Because we did not test every child for RD, it is possible for our study results to be biased if boys and girls were differentially referred for testing. However, our data suggest that boys were not differentially referred for testing at a higher rate than girls in our study population. In our study, 1,951 children were initially identified as having some type of school problem (1,196 boys and 755 girls). While more boys than girls were initially identified as having school problems, 498 girls and 847 boys received individual IQ and achievement testing (OR = 1.25, 95 percent CI: 0.82, 1.52). Among the children who were not initially identified as having a school problem (1,760 boys and 2,007 girls), 61 girls and 65 boys received IQ and achievement testing (OR = 1.22, 95 percent CI: 0.86, 1.74). Thus, in our study population, boys seemed to be slightly (but not significantly) more likely to be referred for further testing, and these increases were probably not sufficient to appreciably affect our study findings.

Finally, because we did not test every child in our cohort for RD, it is also possible that we may have failed to identify some cases of RD. If we failed to identify approximately equal numbers of girls and boys, our results would underestimate any associations that might truly exist and would be a conservative estimate of associations between risk factors and RD. It is also possible that we may have failed to identify more girls than boys as having RD. However, sensitivity analyses suggest that our observed male-female differences were not due to unidentified RD cases among girls. By applying our observed incidence rate among boys (2.16/1,000 person-years, using the most conservative method for RD identification—the Minnesota regression formula) to the total number of person-years among the girls (39,556.65 person-years), if the risk for RD was equal in boys and girls, we would predict 85.3 RD cases among the girls. Because we identified 26 cases among the girls (by the Minnesota regression formula), we would have needed to miss at least 59 (69 percent) RD children among the remaining girls in the cohort without missing any additional cases among the remaining boys. We believe this is highly unlikely, given our efforts at complete ascertainment.

In conclusion, this study examines the interaction between sex and potential risk factors for RD. Our results suggest that boys and girls are significantly and differentially susceptible to potential risk factors for RD. Therefore, the biologic processes that lead to RD may be different for boys and girls. While further studies are needed to define how genetic, social, and other biologic factors may interact to contribute to the increased level of RD observed in male children compared with female children, our results suggest that boys and girls with RD may need to be considered separately in future RD studies.

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