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Gender, ADHD, and Reading Disability in a Population-Based Birth Cohort

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Abstract

Objective—This study determined the incidence of reading disability (RD) among children with and without research-identified attention-deficit/hyperactivity disorder (ADHD), separately by gender, in a population-based birth cohort.

Method—Subjects included all children born 1976–1982 remaining in Rochester, MN after age five (n = 5718). Information from medical, school, and private tutorial records was abstracted. Cumulative incidence of RD, by any of three RD formulas, in children with and without ADHD and corresponding hazard ratios (HR) were calculated separately by gender.

Results—Cumulative incidence of RD by age 19 was significantly higher in children with ADHD (51% in boys, 46.7% in girls) compared to those without ADHD (14.5% in boys, 7.7% in girls). Among children with ADHD, the risk for RD was similar in boys vs. girls (HR=1.0). However, among children without ADHD, boys were 2.0 times more likely than girls to meet RD criteria. Among girls, the HR for the risk for RD associated with ADHD (vs. non-ADHD) was 8.1 (95% CI 5.7–11.5); this was significantly higher than the corresponding HR among boys (3.9, 95% CI, 3.2–4.9).

Conclusions—The risk for RD is significantly greater among ADHD children compared to non-ADHD children. Among ADHD children, the risk for RD is the same for both boys and girls. However, among non-ADHD children, boys are more at risk for RD than girls. Among girls, the magnitude of increased risk for RD associated with ADHD is nearly twice that among boys because non-ADHD girls are less likely to have RD than non-ADHD boys.

Keywords

ADD; ADHD; Dyslexia; Reading disability; Comorbidity; Epidemiology

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INTRODUCTION

Attention deficit/hyperactivity disorder (ADHD) characterized by developmentally inappropriate and disabling levels of inattentiveness, and/or hyperactivity/impulsivity is often accompanied by associated learning problems.[1] It is not surprising that children with ADHD have difficulties in learning as their inattentive, and/or hyperactive/impulsive behaviors in school may impede their academic productivity. While it has also been thought that specific learning disabilities (LD), such as reading disability (RD) or dyslexia, occur more commonly in children with ADHD than in those without,[2] results of previous studies focusing on the comorbidity between ADHD and LDs (including RD) have been inconsistent.[1–7] This is primarily due to inconsistency in the diagnostic threshold for RD among studies.[1, 8] Furthermore, because most of these studies involved clinically referred samples, results may have been influenced by referral bias. For instance, if children having both ADHD and RD are more likely to be referred due to increased difficulties in school compared to those with only ADHD or RD, the observed comorbid rate between ADHD and RD might be overestimated. As disruptive behaviors of boys with ADHD might lead to increased referrals compared to girls with less disruptive behavior, an overestimation of the male/female ratio may occur in studies of clinic-referred samples. However, Willcutt et al. conducted a series of twin studies regarding comorbidity between ADHD and RD, and concluded that these disorders co-occur more frequently than expected by chance even in community samples.[9–11] In these studies, teachers and parents rated ADHD symptoms. However, as the authors acknowledged,[2, 9] the possibility remains that parents or teachers may be more likely to endorse ADHD symptoms when they know that the child is experiencing difficulty in learning to read. Furthermore, the characteristics of the twin study design do not always reflect those of the general population.

To address limitations of prior studies, we evaluated the incidence rate of research-identified RD among children with and without research-identified ADHD in children from a population-based birth cohort, with explicit assessment of gender differences in the comorbidity between these two disorders.

METHODS

Study Setting and Data Source

Rochester, Minnesota is 90 miles southeast of Minneapolis-St Paul, the closest major urban center. In 1990, when subjects in this birth cohort were school-aged children, there were 70,745 residents who were 96% white, fairly young (72% ≤45 years old), and primarily middle class. The demographic characteristics of Olmsted County (Rochester Standard Metropolitan Statistical Area) residents resembled those of the US white population during the timeframe relevant to this study.[12]

The capacity for population-based epidemiologic research on RD and ADHD in Rochester is the result of a unique set of circumstances. First, Rochester is relatively isolated in southeastern Minnesota, and as a result, virtually all medical care is provided locally by Mayo Clinic and Olmsted Medical Center and their three affiliated hospitals. Through the Rochester Epidemiology Project, all diagnoses and surgical procedures recorded at the Rochester medical facilities are indexed for automated retrieval.[12, 13] The medical record includes a detailed history of all encounters in the community, including psychiatry, psychology reports and psychological test results from birth until patients no longer reside in the community. Second, through a contractual research agreement, all 41 public, parochial and private schools in Minnesota Independent School District (ISD) No. 535, the school system for the city of Rochester, MN, gave us permission to access their richly documented cumulative educational records for every child from our birth cohort. These cumulative

school records are permanently maintained for all children who have attended public, private or home school in the district. Third, under a separate research agreement we also obtained permission to access the resources of the privately owned Reading Center/Dyslexia Institute of Minnesota (the only private tutoring agency in existence in the community during the school years of our birth cohort members), as well as of the only private community psychiatric practice in the area. The study was approved by the Institutional Review Boards of Mayo Clinic and Olmsted Medical Center.

Birth Cohort

Our birth cohort consisted of all children born between January 1, 1976 and December 31, 1982 to mothers residing in the townships comprising Minnesota ISD No. 535 (n = 8458). The target population consisted of 5718 children (2956 boys and 2762 girls) who still lived in Rochester at or after the age of five[14, 15] who were followed retrospectively from birth until the initial occurrence of either death, emigration, or high school graduation. The steps and resources used for identification and follow-up of this birth cohort, and analysis of potential influence of migration bias, have been previously reported.[16]

RD and ADHD Incidence Cases - Identification and Case Definition

Our strategy in identifying all RD and ADHD incidence cases consisted of several steps, used multiple sources of information and relied on recorded history of symptoms, individual test results, and treatment, available for all members of the birth cohort. The details of the case-identification procedures were previously described in detail.[14,15] In short, several steps were used to narrow the pool of potential RD and ADHD incidence cases, starting with cumulative school records of each child in the birth cohort (n = 5718). School records were searched for any indication of concerns about learning and behavior and 1961 children had those concerns observed by teachers, parents, school psychologists, physicians, social workers, and school nurses. Further work on these 1961 children consisted of abstracting data from the school, medical records and the records from two other private facilities described above.

The following data were abstracted: all individually administered academic achievement and cognitive ability test results and detailed information related to behavioral problems (symptoms, clinical diagnoses, results from teacher/parent questionnaires, medication treatment). Identification of RD incidence cases consisted of applying three psychometric criteria. Specifically, for each child designated with learning/behavioral concern, all reading achievement and IQ test scores were used to form pairs of cognitive ability and reading performance measure within each calendar year. The details of the three formulas were previously published.[14] In short, in each of the formulas, x represents the study subject's IQ score, and y represents the standard score from the reading achievement test. Children classified as having RD by the Regression Formula-Minnesota[17] ($y < 17.40 + 0.62\,x$) had standard scores in reading achievement that were >1.75 SD below their predicted standard score from an individually administered measure of cognitive ability (IQ). In the Discrepancy Formula approach, differences between age-based standard scores of measures of individually administered intelligence and reading achievement varied by grade (i.e., $x - y \geq 15$, 19, or 23 points, for kindergarten-3rd, 4th–6th, and 7th –12th grade, respectively). Finally, the Low-Achievement Formula ($x \geq 80$ and $y \leq 90$) represents an alternative method to identify RDs.[18–20]

Identification of ADHD incidence cases consisted of applying research criteria to the 1961 children (34% of the birth cohort) from our birth cohort who had any recorded behavioral or learning concerns. Subjects were defined as research-identified ADHD incidence cases if their school and/or medical records included various combinations of the following three

different categories of information: 1) meets DSM-IV criteria for ADHD, 2) positive ADHD questionnaire results,[21] 3) clinical diagnosis of ADHD (with or without specific subtype) was documented. Details of information regarding those criteria as well as identification process of ADHD cases were described elsewhere.[15] A total of 379 ADHD cases were identified (Table 1).

Non-ADHD Subjects

All the members of the population-based birth cohort who still lived in Rochester at or after the age of five, who were not identified as ADHD incidence cases, and who did not have severe intellectual disability, were designated as non-ADHD subjects.

Statistical Analysis

The Kaplan-Meier method was used to calculate the probability of not meeting the RD criteria from birth to 19 years of age, taking into account the varying duration of each subject's follow-up. In the absence of competing risks, the cumulative incidence of RD was calculated as 1 minus the Kaplan-Meier probabilities and plotted versus age (Fig 1, Fig 2). Children were classified as having RD by any of the three formulas upon the date when they initially met the criteria for one of the three RD formulas. Children who did not meet research criteria for RD were censored on the initial occurrence of migration from the community, death, last follow-up date, or at 19 years of age.

Cox proportional hazards model was applied to obtain hazard ratios and corresponding 95% confidence intervals (CIs). In each Cox model, incidence of RD was regarded as the outcome variable whereas ADHD (cases versus non-cases) and gender (boys versus girls) were regarded as explanatory variables. The assumptions of proportional hazards was assessed by graphical methods (plotting the scaled Schoenfeld residents versus ranked time) and by introducing a time-dependent coefficient in the Cox models. Both unadjusted and adjusted hazard ratios were calculated. In the latter case, children's race (white vs. non-white), mother's educational level and age at birth of child were found to be significantly different between ADHD and non-ADHD subjects (Table 2), and considered to be possibly confounding for the incidence of RD. Therefore, these factors were included in the model. Father's educations level was not included in the model due to the number of missing values, which may not be missing at random. *P*-values (two-sided) less than 0.05 were considered statistically significant.

RESULTS

Among the 5718 subjects in the birth cohort, 19 subjects with severe intellectual disability were excluded, leaving 5699 subjects for the analysis. A total of 379 children fulfilled the research criteria for ADHD at a mean (SD) age of 10.4 (3.6) years (median 9.8 years).

Demographic and perinatal factors obtained from the birth certificate of children with and without ADHD in the birth cohort are shown in Table 2. Subjects with ADHD were significantly more likely to be male ($P < 0.001$), Caucasian ($P = 0.036$), have parents with less years of education ($P = 0.001$ for fathers, and 0.002 for mothers), and have younger mothers at birth ($P = 0.004$), compared to subjects without ADHD. There were no statistically significant differences regarding perinatal factors between those with and without ADHD.

The cumulative incidence of RD identified by any of the three formulas, in boys and girls, as well as the hazard ratio for boys versus girls, separately for those with and without ADHD, are shown in Table 3. In the ADHD group, the cumulative incidence of RD was similar

between boys and girls, while among children without ADHD, boys showed approximately a two-fold cumulative incidence of RD compared to girls (Fig 1).

Table 4 and Fig 2 show the risk of RD incidence associated with ADHD, separately by gender. ADHD was significantly associated with an increased risk of RD in both genders. However, the risk of RD associated with ADHD was significantly higher in girls than in boys (approximately twice as high as boys), as shown by the significant ADHD × gender interaction on the incidence of RD ($P = 0.001$ in the adjusted model). In children with ADHD, the cumulative incidences of RD by age 19, separately for the three RD formulas, ranged from 21.1% to 43.2% for boys and from 19.5% to 43.4% for girls.

DISCUSSION

Population-based, non-referred samples of boys and girls with ADHD and RD are of critical importance in order to increase our understanding of the natural history of the comorbidity between ADHD and RD. The core of this epidemiologic study is the population-based sample of carefully defined, research-identified ADHD and RD incidence cases.

Our primary findings are:

1. The cumulative incidence of RD is (a) higher in children with ADHD than in those without ADHD in both genders, and (b) there is a significant ADHD × gender interaction on the incidence of RD. Thus, the risk of RD associated with ADHD is higher in girls than in boys.
2. Among children with ADHD, both genders show similar cumulative incidence rates of RD, while the cumulative incidence rates of RD are higher in boys than in girls among children without ADHD.

In previous studies using clinic-referred samples, the diversity of definitions used to diagnose RD has resulted in inconsistent reports of the comorbidity between ADHD and RD.[1] We employed three formulas for determining RD incidence. The cumulative incidence rate of RD by 19 years of age in children with ADHD identified by each of the three formulas in our population-based birth cohort fell in the range of 20%–43% for both genders, which is fairly consistent with the previous studies of clinical samples selected for ADHD, [1, 2] and those by Willcutt et al.[9, 11] In addition, our population-based study showed an overall approximate 50% cumulative incidence rate of RD (identified by any of the three formulas) in children with ADHD for both genders. Thus, the comorbidity between ADHD and RD in our community sample was as high as previously reported in clinical samples.

Although the cumulative incidence of RD in boys was twice as high as in girls among children *without* ADHD, the similar incidence rates of RD between boys and girls among children *with* ADHD suggests that ADHD is more strongly associated with RD in girls. This means that both boys and girls with ADHD are at high risk to be affected by RD. The relative preponderance of ADHD subtypes has been reported to vary greatly based on gender.[22–25] Furthermore, the comorbidity of ADHD and RD has been reported to vary according to ADHD subtype.[10, 11, 26] Willcutt et al.[10] found that the inattentive symptoms of ADHD were more strongly associated with RD than the hyperactive-impulsive symptoms in a community sample. However, they also implied that the relationship between RD and ADHD subtypes are likely to be complex, and therefore, warrant additional research.[9] Moreover, recent studies of ADHD subtypes suggest a lack of stability of subtypes over time and thus question their validity as categorical diagnoses.[27–29] The retrospective nature of this study and changes in the terms of ADHD subtype over time prevented us from obtaining precise information about ADHD subtype for our subjects, and we are therefore unable to

address the issue of the influence of ADHD subtype on the extent of comorbidity between ADHD and RD.

Recently, both ADHD and RD have been found to be strongly influenced by genetic factors.[11, 26, 30] Candidate gene and linkage studies of RD and ADHD have suggested the presence of common genes contributing to both disorders.[2] There is no additional evidence to support that two disorders are transmitted independently in families.[31, 32] These findings suggest that both RD and ADHD are disorders based, at least in part, on common genetic etiological factors that increase susceptibility to the comorbidity of both disorders.

Several limitations should be considered when interpreting the present results. First, it should be noted that it was not possible for us to determine whether symptoms of ADHD preceded those of RD. As this investigation is a retrospective cohort study in which the relevant information regarding diagnoses depended on retrospective review of medical and school records, the precise age of onset of both ADHD and RD among children in our sample was not possible to determine; rather, we were able to determine the age at which sufficient information had been documented in the medical and school records to fulfill research criteria for RD and ADHD. It is also possible that some RD or ADHD cases remained unidentified because no screening measures were performed on every child in our birth cohort. However, it should be emphasized that for every child in the birth cohort a systematic, multistaged, multi-resource process was implemented to identify 1961 children (34% of the birth cohort) who had learning behavior concerns. In addition, we uniformly applied clearly defined research criteria for the identification of all incident cases of ADHD and RD, regardless of gender.[14, 15] Finally, at the time of the study Rochester, Minnesota was primarily a white, middle class community so inferences to other populations or settings may be limited. However, Rochester has no access problems to medical care and a homogeneous population (95% white) thereby minimizing the confounding effect of ethnicity and race on the study questions.

CONCLUSIONS

This population-based birth cohort study demonstrates that the incidence of RD is significantly higher in children with ADHD than in those without ADHD in both genders. However, the risk of RD associated with ADHD is significantly higher in girls than in boys. This implies that ADHD is more strongly associated with RD in girls than in boys. In the future, epidemiologic and genetic studies with larger population-based prospective designs and more clearly delineated subtypes of ADHD will lead to a more thorough understanding of the gender differences in the comorbidity between ADHD and RD. Although the American Academy of Pediatrics clinical practice guideline on the diagnosis and evaluation of children with ADHD does not specifically recommend psychoeducational testing for every child with ADHD,[33] our findings clearly demonstrate that it is essential for clinicians to assess all children with ADHD for the presence of comorbid RD.

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Abbreviations

ADHD	Attention Deficit Hyperactivity Disorder
LD	Learning disability
RD	Reading disability
ISD	Independent School District
DSM	Diagnostic and Statistical Manual of Mental Disorders
IQ	Intelligence Quotient
CI	Confidence Interval
HR	Hazard Ratio

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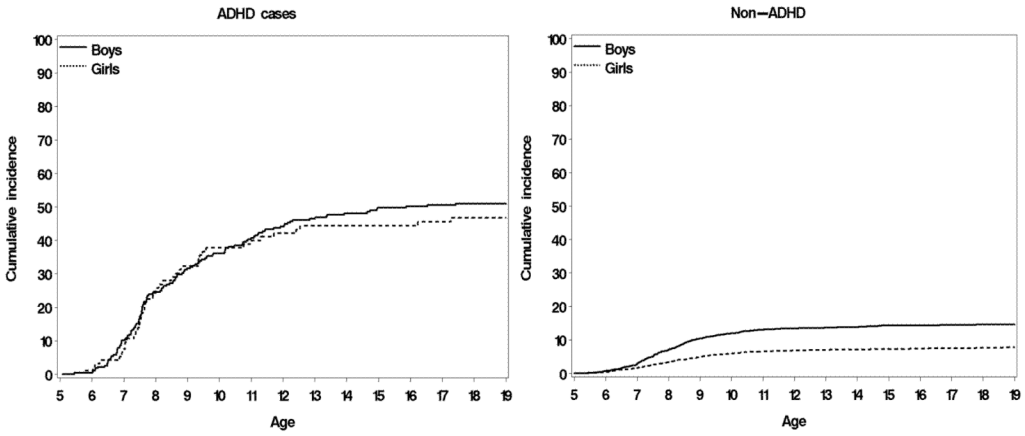

Figure 1.
Cumulative incidence rates of RD identified by any of three formulas for boys and girls, separately by ADHD status.

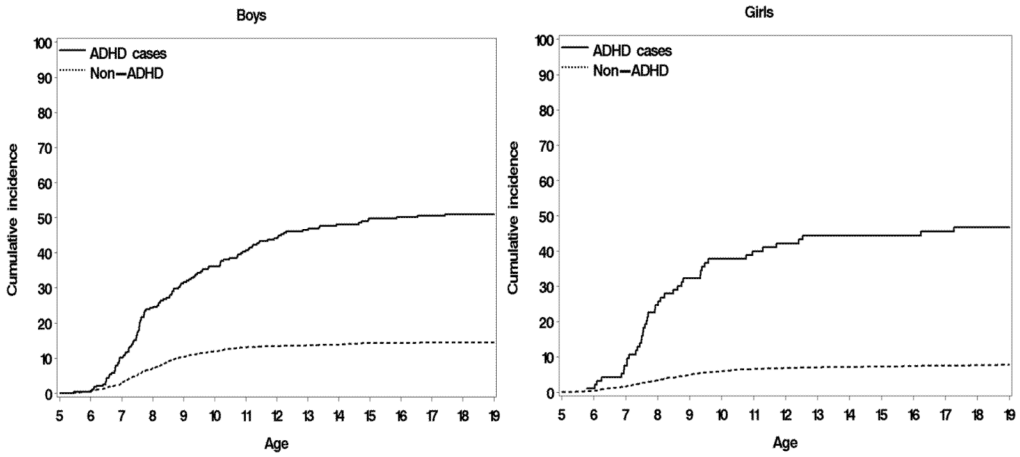

Figure 2.
Cumulative incidence rates of RD identified by any of three formulas for children with and without ADHD, separately by gender.

TABLE 1

Research Criteria for ADHD Case Definition

ADHD Cases	Meets[a] DSM-IV Research Criteria for ADHD	ADHD Questionnaire Results	Clinical Diagnosis of ADHD[b]	Number of Subjects	
Research identified ADHD cases	+	+	+	170	
	+	+	--	41	
	+	--	+	17	228
	--	+	+	122	
	--	--	+	29	151
					379

Pluses and minuses indicate the presence or absence, respectively, of a given criterion.

[a] All DSM-IV criteria were met, only age criterion was not used.

[b] Clinical diagnosis of ADHD (with or without subtype) was recorded in the medical record.

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TABLE 2

Demographic and Perinatal Factors[a] between Children with and without ADHD

	N missing	ADHD (N=379)	Non-ADHD (N=5320)	*P*-value
Factors of the child				
Boys, *n* (%)	0	284 (74.9)	2666 (50.1)	<0.001
White, *n* (%)	6	376 (99.2)	5182 (97.5)	0.036
Birth weight <2500 mg, *n* (%)	11	16 (4.2)	233 (4.4)	0.88
Paternal/Maternal Factors at Birth				
Father's years of education, *n* (%)	786			0.001
<12		22 (6.9)	208 (4.5)	
12		121 (38.1)	1415 (30.8)	
13–15		75 (23.6)	1053 (22.9)	
16+		100 (31.5)	1919 (41.8)	
Mother's years of education, *n* (%)	494			0.002
<12		29 (8.4)	315 (6.5)	
12		138 (40.1)	1662 (34.2)	
13–15		116 (33.7)	1594 (32.8)	
16+		61 (17.7)	1290 (26.5)	
Father's age, mean (SD)	291	28.6 (5.5)	28.0 (5.3)	0.39
Mother's age, mean (SD)	0	25.9 (4.8)	26.6 (4.7)	0.004
Father White, *n* (%)	215	360 (99.5)	5022 (98.1)	0.057
Mother White, *n* (%)	6	377 (99.5)	5203 (97.9)	0.035
Marital status, *n* (%)	1			0.12
Married		345 (91.0)	4953 (93.1)	
Not married		34 (9.0)	366 (6.9)	
Pregnancy/Labor/Delivery Factors				
Pregnancy complications, *n* (%)	0	37 (9.8)	432 (8.1)	0.26
Labor/delivery complications, *n* (%)	0	135 (35.6)	1945 (36.7)	0.71
Congenital anomalies, *n* (%)	0	5 (1.3)	35 (0.7)	0.14

[a]Computerized birth certificate information (continuous and dichotomous variables) for all birth cohort children were obtained from the Minnesota Department of Health.

TABLE 3

Risk of RD[a] Associated with Gender, Separately by ADHD Status

	N	Number of RD cases by age 19	Cumulative incidence by age 19, % (95%CI)	Unadjusted HR[b] (95% CI), *P*-value	Adjusted HR[c] (95% CI), *P*-value
ADHD					
Boys	284	137	51.0 (44.5–56.6)	1.10 (0.78–1.55), 0.58	1.04 (0.73–1.50), 0.83
Girls	95	43	46.7 (35.5–56.0)	1.00	1.00
Non-ADHD					
Boys	2666	332	14.5 (13.0–15.9)	1.97 (1.64–2.36),<0.001	2.03 (1.67–2.45), <0.001
Girls	2654	176	7.7 (6.6–8.8)	1.00	1.00

HR, hazard ratio for boys vs. girls.

[a]RD, reading disability as determined by any of the three formulas.

[b,c]There is a statistically significant difference between the HR (for boys vs. girls) among ADHD children and that among non-ADHD children ($P = 0.003$ in the unadjusted model and $P = 0.001$ in the adjusted model).

[c]Adjusted for children's race (white v. non-white), mother's educational level (four categories) and mother's age at birth of child.

TABLE 4

Risk of RD[a] Associated with ADHD, Separately by Gender

	N	Number of RD cases by age 19	Cumulative incidence by age 19, % (95%CI)	Unadjusted HR[b] (95% CI), *P*-value	Adjusted HR[c] (95% CI), *P*-value
Boys					
ADHD	284	137	51.0 (44.5–56.6)	4.27 (3.50–5.21), <0.001	3.94 (3.19–4.85), <0.001
Non-ADHD	2666	332	14.5 (13.0–15.9)	1.00	1.00
Girls					
ADHD	95	43	46.7 (35.5–56.0)	7.73 (5.54–10.80),<0.001	8.13 (5.73–11.54),<0.001
Non-ADHD	2654	176	7.7 (6.6–8.8)	1.00	1.00

HR, hazard ratio for ADHD vs. Non-ADHD.

[a]RD, reading disability as determined by any of the three formulas.

[b,c]There is a statistically significant difference between the HR (for ADHD vs. non-ADHD) among boys and that among girls ($P = 0.003$ in the unadjusted model and $P = 0.001$ in the adjusted model).

[c]Adjusted for children's race (white v. non-white), mother's educational level (four categories) and mother's age at birth of child.