

Twin Study of the Etiology of Comorbidity Between Reading Disability and Attention-Deficit/Hyperactivity Disorder

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This study utilized a sample of 313 eight- to sixteen-year-old same-sex twin pairs (183 monozygotic, 130 dizygotic) to assess the etiology of comorbidity between reading disability (RD) and attention-deficit/hyperactivity disorder (ADHD). RD was assessed by a discriminant function score based on the Peabody Individual Achievement Test, a standardized measure of academic achievement. The DSM-III version of the Diagnostic Interview for Children and Adolescents was used to assess symptoms of ADHD, and separate factor scores were computed for inattention and hyperactivity/impulsivity (hyp/imp). Individuals with RD were significantly more likely than individuals without RD to exhibit elevations on both symptom dimensions, but the difference was larger for inattention than hyp/imp. Behavior genetic analyses indicated that the bivariate heritability of RD and inattention was significant ($h^2_{g(RD/Inatt)} = 0.39$), whereas the bivariate heritability of RD and hyp/imp was minimal and nonsignificant ($h^2_{g(RD/Hyp)} = 0.05$). Approximately 95% of the phenotypic covariance between RD and symptoms of inattention was attributable to common genetic influences, whereas only 21% of the phenotypic overlap between RD and hyp/imp was due to the same genetic factors. *Am. J. Med. Genet. (Neuropsychiatr. Genet.)* 96:293–301, 2000. © 2000 Wiley-Liss, Inc.

KEY WORDS: ADHD; reading disability; comorbidity; twin study

INTRODUCTION

Reading disorder (RD) and attention-deficit/hyperactivity disorder (ADHD) are two of the most common disorders of childhood, each occurring in approximately 5% of the population [American Psychiatric Association, 1994; Shaywitz et al., 1990]. ADHD and RD also co-occur significantly more frequently than expected by chance. Specifically, the rate of RD in samples selected for ADHD typically falls between 25 and 40% [e.g., August and Garfinkel, 1990; Semrud-Clikeman et al., 1992], whereas 15–35% of individuals with RD also meet criteria for ADHD [Gilger et al., 1992; Shaywitz et al., 1995; Willcutt and Pennington, forthcoming]. Moreover, this comorbidity is present in both clinical and community samples, indicating that it is not a selection artifact.

Whereas these previous studies provide convincing evidence for significant comorbidity between RD and ADHD, the etiology of this association is less clear. The twin study design can help to clarify the nature of the relationship between RD and ADHD by identifying the etiological influences that contribute to each disorder considered separately, as well as the overlap between the two disorders. Previous studies suggest that both RD and ADHD are significantly attributable to genetic influences. Estimates of heritability, the proportion of the phenotypic variance that is attributable to genetic influences, range from 0.4 to 0.6 for RD [DeFries and Alarcón, 1996; Light et al., 1995; Stevenson et al., 1993] and from 0.6 to 0.9 for ADHD [Gjone et al., 1996; Levy et al., 1997; Sherman et al., 1997; Stevenson, 1992; Thapar et al., 1995; Willcutt et al., forthcoming].

Based on the finding that RD and ADHD are significantly heritable, several studies have utilized twin data to test whether the same genetic influences contribute to both RD and ADHD. Gilger et al. [1992] conducted cross-concordance analyses with a small sample of twins selected for RD, and found that ADHD and RD were primarily attributable to independent genetic factors. However, a statistical trend suggested that children with comorbid RD and ADHD might represent an etiological subtype. This finding led the authors to conclude that although most cases of RD or ADHD were not attributable to the same genetic influences, some cases of comorbid RD and ADHD might represent a

Contract grant sponsor: NICHD; Contract grant numbers: HD-11681, HD-27802; Contract grant sponsor: NIMH; Contract grant numbers: F32 MH12100, MH00419, MH38820.

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Received 29 July 1999; Accepted 1 October 1999

separate disorder with a genetic etiology distinct from that associated with either diagnosis in isolation.

Light et al. [1995] and Stevenson et al. [1993] expanded on the findings of Gilger et al. [1992] by utilizing a more powerful multiple regression technique to estimate the bivariate heritability of ADHD and reading [Light et al., 1995] or spelling difficulties [Stevenson et al., 1993]. In a sample of twins selected because at least one member of the pair met criteria for RD, Light et al. [1995] found significant bivariate heritability for RD and ADHD ($h^2_{g(RD/ADHD)} = 0.45$). In a separate community sample of twins, Stevenson et al. [1993] reported that the bivariate heritability of spelling deficits and ADHD was similar whether probands were selected due to spelling difficulties ($h^2_{g(Spel/ADHD)} = 0.21$) or elevations of ADHD symptoms ($h^2_{g(ADHD/Spel)} = 0.15$), but that these estimates were not statistically significant. In sum, these previous studies provide tentative support for the hypothesis that comorbidity between reading or spelling disability and ADHD may be attributable to common genetic influences. These findings are somewhat inconclusive, however, because most estimates of bivariate heritability were only marginally significant.

Potential Influence of Subtypes of ADHD

Interpretation of previous twin studies of the relation between RD and ADHD is complicated by the multiple changes in the diagnostic criteria for ADHD during the past two decades. The studies described previously utilized broadband measures of ADHD such as the Diagnostic Interview for Children and Adolescents [DICA; Herjanic and Reich, 1982] and the Rutter questionnaire [Rutter, 1970]. In contrast to this unidimensional conceptualization of ADHD, more recent exploratory and confirmatory factor analyses have consistently indicated that symptoms of ADHD are best described by two factors consisting of symptoms of hyperactivity/impulsivity (hyp/imp) and symptoms of inattention [Bauermeister, 1992; Burns et al., 1997a, 1997b; Conners et al., 1998a, 1998b; DuPaul et al., 1997, 1998; Hudziak et al., 1998; Pelham et al., 1992; Sherman et al., 1997].

Studies of the external validity of these two dimensions have shown that in comparison with children with elevations on both of these dimensions, children with a specific elevation of symptoms of inattention are more likely to meet criteria for a learning disability, to have a family history of learning problems, and to exhibit sluggish cognitive processing [Barkley et al., 1990; Goodyear and Hynd, 1992; Hynd et al., 1991; Lahey et al., 1988; Lahey et al., 1985]. Moreover, a reanalysis of data from the fourth edition *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV) field trials for the disruptive behavior disorders [Lahey et al., 1994] indicated that the number of inattentive symptoms was significantly related to parent ratings of homework problems and teacher ratings of school difficulties, whereas the number of hyp/imp symptoms was not significantly associated with either measure [Lahey and Willcutt, 1998]. Similarly, previous analyses of a subset of the present sample indicated that

whereas children with RD exhibited elevations of both hyp/imp and inattention in comparison with children without RD, the relation was stronger for symptoms of inattention [Willcutt and Pennington, forthcoming].

Taken together, these findings suggest that the relationship between RD and ADHD is stronger for symptoms of inattention than symptoms of hyp/imp. The inclusion of both inattention and hyp/imp symptoms in an overall composite might mask any effects that were associated with only one of the dimensions. Therefore, the present study was designed to extend previous research in three ways. First, the present sample is substantially larger than the samples utilized in previous twin studies of comorbidity between RD and ADHD, providing greater statistical power to test whether RD and ADHD are coheritable. Second, results of a previous principal axis factor analysis were used to compute factor scores for inattention and hyp/imp, facilitating a direct test for differences in the etiology of the relationship between RD and each symptom dimension. Finally, gender and overall cognitive ability were included in the models to test whether the etiological relation between RD and ADHD differed as a function of these variables.

MATERIALS AND METHODS

Participants

For these analyses, 313 same-sex pairs of 8–16 year-old twins from the ongoing Colorado Learning Disabilities Research Center [DeFries et al., 1997] were used. The sample consisted of 183 monozygotic (MZ) twin pairs (99 male, 84 female) and 130 dizygotic (DZ) pairs (71 male, 59 female) selected because at least one member of the pair met the criteria for RD. In addition, a comparison sample of 510 twins was selected from pairs in which neither twin had a history of significant reading problems for phenotypic comparisons of the prevalence of ADHD among participants with and without RD.

Zygoty Determination

Zygoty of the twins was determined using a modified version of the zygoty questionnaire described by Nichols and Bilbro [1966]. This questionnaire has been shown to classify 96% of twins reliably. If zygoty classification was ambiguous based on the questionnaire, DNA polymorphisms obtained from blood plasma or cheek samples were compared between twins to ensure accurate categorization.

Measure of Reading Disability

The DSM-IV definition of “reading disorder” (RD) specifies that an individual’s academic achievement must not only fall significantly below the achievement typical of other children of the same age, but must also be discrepant from the achievement that would be predicted based on the individual’s overall cognitive ability. However, several studies have suggested that the same etiological factors and neurocognitive deficits are associated with RD with and without an IQ discrepancy, and that the inclusion of an IQ discrepancy as a

diagnostic criterion adds little to the external validity of the diagnosis [Pennington et al., 1992; Siegel, 1989]. On the other hand, a recent twin study found that the heritability of RD increased as a linear function of IQ, suggesting that IQ differences may be relevant to the definition of RD [Wadsworth et al., forthcoming]. Because this controversy has not been resolved conclusively, analyses were conducted separately using the age-discrepancy criterion described in following paragraphs and an IQ-discrepancy formula that was utilized in previous studies of the relation between RD and ADHD [Frick et al., 1991]. Virtually identical results were obtained using these two methods, so only the findings based on the age-discrepancy criterion are reported here.

The Peabody Individual Achievement Test [PIAT; Dunn and Markwardt, 1970] was used to assess academic achievement in reading and spelling. The PIAT manual reports adequate test-retest reliability, and the construct validity of the measure has been demonstrated by significant correlations with other measures of academic achievement and with parent and teacher reports of school performance [e.g. Baum, 1975; Ollendick et al., 1975]. A discriminant function analysis conducted in separate samples of nontwin individuals with and without a history of significant reading problems was used to create a normally distributed reading composite score based on each subject's scores on the reading recognition, reading comprehension, and spelling subtests [DeFries, 1985]. As recommended by Reynolds [1984], RD was defined by a cutoff score 1.65 standard deviations below the mean of a separate sample of control twins without a school history of reading problems. This cutoff selects approximately 5% of the control sample, a prevalence that is consistent with estimates from epidemiological studies [e.g., Shaywitz et al., 1990].

Measure of ADHD

The third edition *Diagnostic and Statistical Manual of Mental Disorders* (DSM-III) [American Psychiatric

Association, 1980] version of the DICA, Parent Report Version [Herjanic and Reich, 1982], was used to assess symptoms of ADHD. The attention deficit disorder subscale of the DICA consists of dichotomous items that assess the 16 symptoms of DSM-III ADHD. The inter-interview reliability of the DICA is reported to be .82, and diagnoses based on the DICA have been shown to be concordant with blind clinical assessments approximately 90% of the time [Welner et al., 1987]. Because maternal report was available for many more children than paternal report (93% of all twins vs. 46% of all twins), maternal report was used for the analyses described in this report. Consistent with the DSM-III and the DICA manual, a cutoff score of eight positive symptoms was used as the diagnostic criterion for the overall diagnosis of ADHD. This cutoff identified 9.6% of a separate comparison sample of 542 twins from pairs in which neither twin had evidence of learning difficulties in their academic records.

Assessment of the Symptom Dimensions of ADHD. Table I provides a summary of a principal axis factor analysis of the DICA conducted as part of a previous study [Willcutt and Pennington, forthcoming]. The inattention and hyp/imp factor scores were utilized for the present analyses. In addition, to facilitate the examination of the etiology of the relation between RD and extreme hyp/imp or inattention scores, extreme inattention and hyp/imp groups were defined based on these factor scores. Because approximately 10% of the comparison sample without learning problems met criteria for the overall diagnosis of ADHD, the 90th percentile of the comparison sample was also used as the extreme-score cutoff on the inattention and hyp/imp factors.

Data Analyses

Concordance and Cross-Concordance Estimates. MZ twins share all of their genes, whereas dizygotic DZ twins share half of their segregating genes on average. Therefore, a significantly higher rate of concordance for a diagnosis between pairs of MZ

TABLE I. Principal Axis Factor Analysis of Symptoms of DSM-III Attention-Deficit/Hyperactivity Disorder (ADHD)

DSM-III domain	Item content	Factor ^a	
		Inattention ^b	Hyp/Imp ^b
Inattention	Often fails to finish things he or she starts	.79	—
Inattention	Often doesn't seem to listen	.71	—
Inattention	Easily distracted	.72	—
Inattention	Has difficulty concentrating on schoolwork	.79	—
Inattention	Has difficulty sticking to a play activity	.35	.36
Impulsivity	Often acts before thinking	—	.60
Impulsivity	Shifts excessively from one activity to another	.74	—
Impulsivity	Has difficulty organizing work	.71	—
Impulsivity	Needs a lot of supervision	.70	—
Impulsivity	Frequently calls out in class	—	.58
Impulsivity	Has difficulty awaiting turn	—	.62
Hyperactivity	Runs about or climbs on things excessively	—	.72
Hyperactivity	Has difficulty sitting still or fidgets excessively	—	.78
Hyperactivity	Has difficulty staying seated	—	.70
Hyperactivity	Moves about excessively during sleep	.28	.44
Hyperactivity	Is always "on the go" or acts as if "driven by a motor"	—	.76

*After Willcutt & Pennington, in press.

^aPrincipal axis factor analysis with direct oblimin rotation with Kaiser normalization.

^bItem loadings in boldface indicate items which were included in the composite score for that factor.

twins than DZ twins would suggest that the disorder is attributable to the influence of genes. For the present analyses all twins who met criteria for RD were selected as probands. For those cases in which both twins from a pair met criteria for RD, the pair was double-entered into the data file (i.e., each member of the pair was entered once as a proband and once as a cotwin). This procedure provides the most valid estimate of twin concordance when a sample has been ascertained using truncate selection [e.g., DeFries and Alarcón, 1996; McGue, 1992].

The DeFries-Fulker Multiple Regression Method. Whereas a comparison of the rates of concordance in MZ and DZ twin pairs provides a conceptually simple appraisal of the etiology of a discrete disorder, the multiple regression method proposed by DeFries and Fulker [DF method; 1985, 1988] provides a more powerful and versatile test of the etiology of extreme scores on a continuous dimension. The DF method is based on the regression of MZ and DZ cotwin scores toward the population mean when probands are selected due to extreme scores on a phenotype. Although scores of both MZ and DZ cotwins would be expected to regress toward the population mean, scores of DZ cotwins should regress further toward the mean of the unselected population than scores of MZ cotwins to the extent that extreme ADHD scores are influenced by genes.

Similar to the concordance analyses, all twins who scored below the cutoff on the reading composite were selected as RD probands for the regression analyses. Because the double entry of concordant pairs artificially inflates the sample size, the standard errors of the regression coefficients were corrected prior to tests of significance [e.g., Stevenson et al., 1993]. Prior to the inception of the multiple regression analysis, standardized scores were created based on the mean and standard deviation of the non-RD sample. The standardized scores for the selected sample of MZ probands and cotwins were then divided by the MZ proband mean, and the DZ proband and cotwin scores were divided by the DZ proband mean. This procedure ensures that the MZ and DZ probands are equally divergent from the mean score of the controls prior to the regression analysis.

The basic regression model for the univariate case is as follows:

$$C = B_1P + B_2R + K \quad (1)$$

where C is the expected cotwin score, P is the proband score, R is the coefficient of relationship (1 for MZ pairs, 0.5 for DZ pairs), and K is the regression constant. The B_1 coefficient represents the partial regression of the cotwin's score on the proband's score, and provides a measure of twin resemblance irrespective of zygosity. The B_2 parameter represents the partial regression of the cotwin's score on the coefficient of relationship, and after appropriate transformation of the data provides a direct estimate of the heritability of extreme scores on the trait under consideration (h^2_g). After adjustment of the standard errors of the regression coefficients to correct for the double entry of concordant pairs, the significance of the B_2 parameter pro-

vides a statistical test of the extent to which extreme scores are attributable to genetic influences.

The Bivariate Case. A simple generalization allows the univariate concordance and multiple regression analyses to be applied to bivariate data [e.g., Light & DeFries, 1995]. Instead of comparing the relative similarity of MZ and DZ twins for the same trait, bivariate analyses compare the relation between the proband's score on one trait and the cotwin's score on a second trait across zygosity. Therefore, if common genetic influences contribute to the association between RD and ADHD, cotwins of MZ probands with RD should be more likely to meet criteria for ADHD than cotwins of DZ probands with RD. Similarly, the ADHD score of the cotwins of MZ probands with RD would be expected to regress less toward the population mean than the ADHD score of DZ cotwins.

The regression equation to apply the DF method to bivariate data is expressed as follows:

$$C_{ADHD} = B_1P_{RD} + B_2R + K \quad (2)$$

where C_{ADHD} is the expected cotwin score on the non-selected measure (ADHD), P_{RD} is the proband score on the selected measure (RD), R is the coefficient of the relationship, and K is the regression constant. The B_2 coefficient provides a direct estimate of the bivariate heritability of RD and ADHD ($h^2_{g[RD/ADHD]}$), the extent to which the proband reading deficit is attributable to genetic influences that are also associated with elevations of ADHD.

The DF model is highly versatile, and can be elaborated to test for the influence of other independent variables on the etiology of the comorbidity under consideration. For example, the model to test for the influence of IQ on the bivariate heritability of RD and ADHD would be as follows:

$$C_{ADHD} = B_1P_{RD} + B_2R + B_3P_{IQ} + B_4P_{IQ} * P_{RD} + B_5P_{IQ} * R + K \quad (3)$$

where C_{ADHD} is the expected cotwin score on the non-selected measure (ADHD), P_{RD} is the proband score on the selected measure (RD), R is the coefficient of relationship, P_{IQ} is the IQ of the proband, $P_{IQ} * P_{RD}$ is the product of the proband's IQ score and the proband's reading score, and $P_{IQ} * R$ is the product of the proband's IQ and the coefficient of relationship. The B_3 term represents a test for the main effect of IQ on the nonselected variable (ADHD), and the B_5 coefficient tests for differential bivariate heritability of RD and ADHD as a function of IQ.

RESULTS

Demographic Characteristics

The familial SES of the RD probands was significantly lower than the SES of the comparison sample [Hollingshead, 1975], but the two groups did not differ significantly in age (Table II). The ethnic composition of the overall sample was 84.8% White, 7.9% Hispanic, 4.0% Black, 1.7% Asian, and 1.1% American Indian, and was not significantly different in the samples of individuals with and without RD. As expected, individuals with RD scored lower on the measures of full-scale IQ (FSIQ) and reading achievement.

TABLE II. Mean Scores on Demographic Variables and Measures of Attention-Deficit/Hyperactivity Disorder (ADHD) in Individuals With and Without Reading Disability (RD)

Measure	Individuals without RD (N = 510)		Individuals with RD (N = 485)		t
	M	SD	M	SD	
Socioeconomic status	27.1	14.9	36.7	16.1	8.14**
Age	11.3	2.7	11.2	2.7	NS
Full scale IQ	114.1	10.3	97.5	10.7	23.25**
Reading discriminant function Z-score	0.12	0.9	-2.79	0.8	50.18**
Total symptoms of DSM-III ADHD	2.13	3.2	5.79	4.7	12.44**
Hyperactive/Impulsive factor Z-score	-0.13	0.8	0.13	1.1	3.68**
Inattention factor Z-score	-0.42	0.8	0.47	1.1	12.92**

** = $p < 0.01$.

Consistent with previous analyses in a subset of the present sample [Willcutt and Pennington, forthcoming], individuals with RD scored significantly higher on all three measures of ADHD than individuals from the control sample. Moreover, categorical analyses indicated that RD probands were more than five times more likely than control participants to meet diagnostic criteria of eight or more positive symptoms of ADHD (34% vs. 6%). To assess the overlap between RD and extreme inattention or hyp/imp, cutoff scores on the hyp/imp and inattention composites were derived to select the same proportion of the control sample as met criteria for the overall diagnosis of ADHD. Individuals with RD were more than seven times more likely to score above the extreme score cutoff on the inattention factor (40% vs. 6%), and almost three times as likely to score above the extreme score cutoff on the hyp/imp factor (17% vs. 6%).

Concordance and Cross-Concordance Rates for RD and ADHD in MZ and DZ Twins

The proband-wise concordance rate for RD was significantly higher for MZ twins (79%) than DZ twins

(52%), suggesting that the diagnosis of RD is significantly attributable to genetic influences. Although a community sample of individuals selected for ADHD was not available in the present study, previous twin studies have consistently obtained higher concordance rates among MZ pairs than DZ twins for the diagnosis of ADHD [e.g., Levy et al., 1997]. Therefore, because RD and ADHD are both attributable to genetic influences, cross-concordance analyses were utilized to test whether the same genetic influences contribute to the significant comorbidity between RD and ADHD in this sample.

The cross-concordance of RD and the overall ADHD diagnosis was significantly higher among MZ twins than DZ twins (Figure 1), suggesting that common genetic influences are associated with both RD and ADHD. However, different results were obtained for the two dimensions of ADHD symptoms. The rate of cross-concordance for RD and extreme inattention was significantly higher in MZ than DZ pairs, whereas the cross-concordance for RD and hyp/imp was nearly identical in MZ and DZ pairs. This result suggests that common genes are associated with RD and extreme

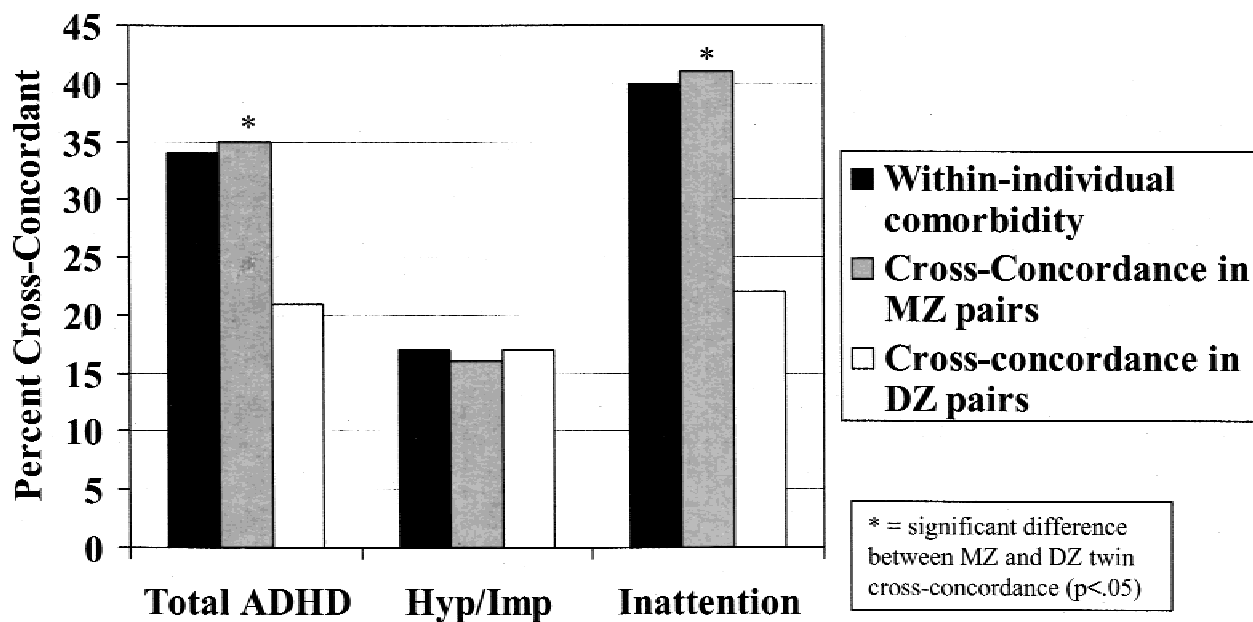


Fig 1. Comorbidity and cross-concordance of RD and ADHD in MZ and DZ twin pairs selected for RD.

TABLE III. Cross-Concordance by Zygosity of Reading Disability and Each Symptom of DSM-III Attention-Deficit/Hyperactivity Disorder

	Percentage exhibiting symptom	
	Monozygous cotwins	Dizygous cotwins
Inattention symptoms		
Often fails to finish things he or she starts	62 ^a	42
Often doesn't seem to listen	39 ^a	23
Easily distracted	62 ^a	40
Has difficulty concentrating on schoolwork	48 ^a	34
Shifts excessively from one activity to another	47 ^a	33
Has difficulty organizing work	53 ^a	33
Needs a lot of supervision	52	46
Hyperactivity/impulsivity symptoms		
Often acts before thinking	22	23
Frequently calls out in class	26	21
Has difficulty awaiting turn	14	13
Runs about or climbs on things excessively	30	26
Has difficulty sitting still or fidgets excessively	18	24
Has difficulty staying seated	26	24
Is always "on the go" or acts as if "driven by a motor"	17	14

^aCross-concordance significantly higher in monozygous than dizygous pairs ($p < .05$).

inattention, whereas RD and extreme hyp/imp are not significantly attributable to the same genetic influences. Interestingly, the rate of within-individual comorbidity was highly similar to the rate of MZ cross-concordance for RD and all three measures of ADHD, suggesting that unshared environmental influences do not contribute to the overlap between RD and ADHD.

To test whether the genetic relation between RD and inattention was restricted to a subset of inattention symptoms, the cross-concordance of RD and each symptom of ADHD was compared by zygosity (Table III). The MZ cross-concordance rate was significantly higher than the DZ cross-concordance for six of the seven inattention symptoms, but was not significantly different for any of the seven symptoms on the hyp/imp factor.

Heritability Estimates

Whereas cross-concordance analyses provide a rough index of the extent to which genetic and environmental influences contribute to the overlap between two disorders, the DF multiple regression method provides a more powerful test of the etiology of this association and facilitates the estimation of the relative influence of genetic and environmental factors. A univariate analysis of the heritability of RD in this sample indicated that reading deficits were significantly heritable, $h^2_g = 0.53(.08)$, $t = 6.63$, $p < .001$. Subsequent bivariate analyses were conducted to test whether ADHD symp-

toms were attributable to the same genetic influences that were associated with RD.

The mean reading composite scores of the MZ and DZ probands each fell more than two and one-half standard deviations below the mean of the control sample (MZ $M = 2.75$, $SD = 0.78$; DZ $M = 2.72$, $SD = 0.80$). Table IV presents the means and standard deviations of the standardized inattention, hyp/imp, and total DICA scores for the cotwins of MZ and DZ probands with RD. The mean standardized DICA score for the MZ cotwins (0.97 standard deviations above the control mean) was more extreme than the mean DICA score for the DZ cotwins (0.66 standard deviations above the control mean), consistent with what would be expected if the same genetic influences contribute to both RD and ADHD. Indeed, results of the multiple regression analysis revealed significant bivariate heritability for the reading composite score and the total number of ADHD symptoms. To test whether the etiology of the association between RD and ADHD was different for the two dimensions of ADHD symptoms, separate multiple regression analyses were conducted to provide estimates of bivariate heritability for RD and symptoms of hyp/imp and inattention. Results revealed significant bivariate heritability for RD and inattention but not for RD and hyp/imp, providing converging evidence in support of the hypothesis that the relation between RD and ADHD may differ by dimension of ADHD.

As a final test of the nature of the relation between

TABLE IV. Summary of Analyses of the Bivariate Heritability of Reading Disability (RD) and Attention-Deficit/Hyperactivity Disorder (ADHD) in Twin Pairs Selected for RD

Cotwin measure	Monozygous cotwins	Dizygous cotwins	Bivariate	t	PG ^a
	Mean (SD)	Mean (SD)	h^2_g (SE)		
DSM-III ADHD	0.97 (1.43)	0.66 (1.35)	.23 (.12)	1.92*	.64
DSM-III Hyp/Imp ^b	0.64 (1.52)	0.57 (1.47)	.05 (.15)	0.34	.21
DSM-III Inattention	1.00 (1.39)	0.47 (1.20)	.39 (.13)	2.99**	.95

^aPG = proportion of phenotypic overlap accounted for by genetic influences.

^bHyp/Imp = hyperactivity/impulsivity.

* = $p < .05$, ** = $p < .01$.

RD and ADHD, the influence of gender and FSIQ was tested by including these variables as moderators in extended DF models. The bivariate heritability of RD and ADHD did not vary significantly as a function of FSIQ for any of the measures of ADHD ($p > .50$). Similarly, bivariate heritability estimates also did not vary significantly as a function of gender, although a statistical trend ($p < .20$) suggested that the overlap between RD and hyp/imp may be more heritable among males ($h^2_{g(RD/Hyp)} = .20$) than among females ($h^2_{g(RD/Hyp)} = -.09$).

Proportion of the Phenotypic Covariance Between RD and ADHD Accounted for by Genetic Influences

Whereas bivariate heritability estimates the extent to which the proband reading deficit is attributable to genetic influences that are also associated with elevations of ADHD, it is also possible to estimate the proportion of the phenotypic covariance between RD and ADHD that is accounted for by the same genes [PG; Stevenson et al., 1993]. In this sample the phenotypic covariance between RD and ADHD was estimated by regressing scores for each measure of ADHD onto the reading composite score. The estimate of PG then was calculated by dividing the estimate of bivariate heritability by the phenotypic covariance of the two dimensions. As seen in the last column of Table IV, 64% of the phenotypic overlap between RD and the entire dimension of ADHD symptoms is attributable to the same genetic influences. However, the etiology of this overlap appears to differ for the two dimensions of ADHD symptoms; 95% of the overlap between RD and inattention was attributable to common genetic influences, whereas only 21% of the overlap between RD and hyp/imp was due to the influence of the same genes.

DISCUSSION

This study utilized a community sample of 8–18 year-old twins to examine the etiology of comorbidity between RD and ADHD. Cross-concordance and bivariate multiple regression analyses indicated that the overlap between RD and ADHD is largely attributable to common genetic influences, but that this relation may be different for the two dimensions of ADHD symptoms. Specifically, the bivariate heritability estimate for RD and scores on the inattention factor was significant ($h^2_{g(RD/Inatt.)} = 0.39$), and 95% of the phenotypic overlap between RD and inattention was attributable to common genetic influences. In contrast, the bivariate heritability for RD and scores on the hyp/imp factor was not significant ($h^2_{g(RD/Hyp)} = 0.05$), and only 21% of the overlap between RD and hyp/imp was attributable to common genes.

Implications of the Present Findings for Competing Explanations for Comorbidity Between RD and ADHD

The present results support most strongly the common genetic etiology hypothesis as an explanation of the etiology of the relation between RD and elevations of inattention. However, several other competing ex-

planations have also been proposed to explain the etiology of the association between RD and ADHD. For example, comorbidity between RD and ADHD could be attributable to a sampling artifact [e.g., Berkson, 1946], cross-assortative mating for the two traits [Faraone et al., 1993], or a causal relation between one disorder and the other [e.g., Pennington et al., 1993].

The sampling artifact hypothesis suggests that before considering competing explanations for the etiology of comorbidity between two disorders, it is prudent to test whether the co-occurrence of the disorders is attributable to a sampling or measurement artifact [Caron and Rutter, 1991]. The present findings converge with results from other community samples to indicate that the association between RD and ADHD is not restricted to clinical samples [e.g., Fergusson and Horwood, 1992], and is therefore not a sampling artifact. The significant comorbidity between RD and ADHD in the present sample also cannot be explained by symptom overlap or common method variance, as the ADHD phenotype was based on parent report whereas the RD phenotype was derived from performance on cognitive tests.

The cross-assortative mating hypothesis [Faraone et al., 1993] suggests that ADHD and RD co-occur more frequently than expected by chance because individuals with ADHD are more likely to reproduce with individuals with RD than would be expected by chance. Significant cross-assortment would increase the genetic resemblance of DZ twins (or of siblings) to more than 0.50 [e.g., Rende and Plomin, 1995]. Since the genetic resemblance of MZ twins cannot be increased beyond 1.00, cross-assortative mating for ADHD and RD would lead to a lower estimate of bivariate heritability and a higher estimate of shared environmental influences common to both dimensions. Therefore, although the cross-assortative mating hypothesis cannot be tested directly in the present sample, the finding of significant bivariate heritability indicates that even if cross-assortative mating is occurring, the overlap between RD and ADHD is also attributable to common genetic influences. One interesting possibility that would be consistent with the current findings would involve cross-assortative mating for RD and hyp/imp but not for RD and inattention. We are currently conducting more extensive phenotypic evaluations of the parents of these twins to facilitate a more direct test of the cross-assortative mating hypothesis in this sample.

The phenocopy hypothesis [Pennington et al., 1993] proposes that RD and ADHD co-occur because the primary disorder causes the phenotypic manifestation of the secondary disorder in the absence of the etiological influences typically associated with the secondary disorder in isolation. This hypothesis is of particular importance for the present analyses, because if having RD or ADHD causes children to exhibit a phenocopy of the other disorder in the absence of the etiological influences typically associated with the secondary disorder, the pattern of results could mimic the pattern indicative of bivariate heritability [Stevenson et al., 1993]. Although the phenocopy hypothesis cannot be tested directly using the DF method, previous analyses of the cognitive profile of individuals with RD and ADHD pro-

vide evidence against this hypothesis [Willcutt et al., manuscript under review]. Specifically, individuals with comorbid RD and ADHD exhibited the cognitive deficits associated with both ADHD and RD, suggesting that neither RD nor ADHD is a secondary consequence of the other disorder in this sample.

SUMMARY AND DIRECTIONS FOR FUTURE RESEARCH

Results of the present study suggest that common genetic influences predispose children to both reading difficulties and elevations of inattention. In contrast, comorbidity between RD and elevations of hyp/imp is not as strongly attributable to common genetic influences. Although neurocognitive analyses of a subset of the present data set provide evidence against the phenocopy hypothesis, future studies could test this hypothesis more directly by fitting a direction of causation model in an unselected sample [e.g., Wadsworth et al., 1995]. Such a study also could be used to test whether the etiology of the relation between reading achievement and ADHD is different in selected versus unselected samples. Finally, future extensions of this research should assess the specific symptoms of DSM-IV ADHD to test whether similar results are obtained for the DSM-IV dimensions and subtypes.

ACKNOWLEDGMENTS

The first author wishes to thank Jeffrey W. Gilger and Jacquelyn G. Light for statistical consultation. The authors wish to extend their gratitude to the school staff and families that participated in the study.

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