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Understanding comorbidity between specific learning disabilities

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Abstract

Current definitions of specific learning disability (SLD) identify a heterogeneous population that includes individuals with weaknesses in reading, math, or writing, and these academic difficulties often co-occur in many of the same individuals. The Colorado Learning Disabilities Research Center (CLDRC) is an interdisciplinary, multisite research program that uses converging levels of analysis to understand the genetic and environmental etiology, neuropsychology, and developmental outcomes of SLDs in reading (RD), math (MD), and writing (WD), along with the comorbidity between these SLDs and other developmental disorders. The latest results from the CLDRC twin study suggest that shared genetic influences contribute to the significant covariance between all aspects of reading (word reading, reading fluency, and reading comprehension) and math (calculations, math fluency, and word problems), and distinct genetic or environmental influences also contribute to weaknesses in each specific academic domain. RD and MD are associated with a range of negative outcomes on both concurrent measures and measures of functional outcomes completed five years after the twins were first assessed. Over the next several years the CLDRC will continue to expand on this work by administering a comprehensive test battery that includes measures of all dimensions of academic achievement that are described in current definitions of SLD and incorporating these measures in new neuroimaging and molecular genetic studies.

Introduction and overview

Current definitions of specific learning disability (SLD) in the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5), the tenth edition of the International Classification of Diseases (ICD-10; World Health Organization, 1992), and the 2004 Individuals with Disabilities Education Improvement Act (IDEA) identify a heterogeneous population that includes individuals with weaknesses in different aspects of reading, math, or writing (American Psychiatric Association, 2013). While some individuals with SLD exhibit a specific weakness in a single academic domain, SLDs in reading (RD), math (MD), and writing (WD) co-occur more often than expected by chance with one another (30 – 60%) and with other disorders such as attention-deficit/hyperactivity disorder (ADHD), a phenomenon known as *comorbidity* (e.g., Badian, 1999; Landerl & Moll, 2010; R. K. Olson et al., 2013; Willcutt, Betjemann, et al., 2010; Willcutt et al., 2013).

The Colorado Learning Disabilities Research Center (CLDRC) is a long-standing interdisciplinary, multisite research program that investigates the genetic and environmental etiologies, neurobiology, neuropsychology, classification, and longitudinal outcomes of SLDs. One of the primary aims of the CLDRC is to understand the causes and consequences of the frequent comorbidity between SLDs. This objective is important for several reasons. The presence of more than one disorder in the same individual makes it difficult to interpret research studies reporting an association between a variable and a specific SLD because it is not clear whether an undetected comorbidity could be contributing to the association. High rates of comorbidity also raise practical questions about whether treatment of one disorder will also improve symptoms of comorbid disorders, or whether treatment approaches should be modified to account for comorbidities. Further, individuals with comorbid disorders often differ in important ways from individuals with a disorder in isolation, with the comorbid group experiencing greater symptom severity, more extensive and severe functional impairment, and poorer long-term outcomes (e.g., Waschbusch, 2002; Willcutt et al., 2007; Willcutt, Pennington, et al., 2010). Finally, the high rates of comorbidity between putatively distinct SLDs directly challenge simple theoretical models of SLDs and the overall concept of *specific* learning disabilities.

The current paper summarizes previous and new results from the CLDRC to provide a succinct synthesis of current knowledge regarding the etiology of SLDs and their comorbidity. After a brief overview of the CLDRC twin study in the subsequent section, we present our latest results regarding the covariance between different dimensions of reading, math, and spelling achievement and comorbidity between categorically-defined RD and MD. The second section then summarizes new analyses that examined the 5-year outcomes of individuals with RD, MD, or both disorders to assess the impact of each SLD and their comorbidity on later academic, behavioral, and socioemotional outcomes. Finally, we report results of behavioral genetic analyses that were conducted to identify the shared and unique genetic and environmental influences that lead to weaknesses in different aspects of reading and math and their covariance. The paper then concludes by describing several key future objectives that will extend the work of the CLDRC by expanding our battery of measures of neuropsychological, behavioral, and psychosocial functioning and incorporating state-of-the-art neuroimaging and molecular genetic methods.

Overview of the CLDRC twin study

Participants

The Colorado Learning Disabilities Research Center (CLDRC) twin study is an ongoing study of the etiology of learning disorders that has included nearly 6,000 participants since the study was first initiated (e.g., DeFries et al., 1997; McGrath et al., 2011; R.K. Olson, Keenan, Byrne, & Samuelsson, 2017; Peterson et al., 2017; Willcutt, Pennington, et al., 2010). Recruitment procedures and exclusion criteria are described in detail in previous papers (e.g., Willcutt, Pennington, Olson, Chhabildas, & Hulslander, 2005; Willcutt et al., 2013), and are summarized more briefly here due to space constraints. All twins between 8 and 18 years of age in 22 local school districts were invited to participate in the initial screening procedures. If either of the twins exhibited a significant history of learning or attentional difficulties during the screening, the pair was invited to participate in the full study (90% of families identified by the screening procedure agreed to participate). Due to the primary focus of the overall study, pairs in which at least one twin exhibited significant learning difficulties were oversampled (approximately 67% of the final tested sample) to increase statistical power for analyses of extreme groups. In addition, a comparison sample was recruited from the remaining twin pairs in which neither twin exhibited a significant history of learning or attentional difficulties. Finally, a subsample of 818 participants from the initial twin study returned for a follow-up assessment that was completed approximately five years after their initial participation (e.g., Wadsworth, DeFries, Olson, & Willcutt, 2007; Wadsworth, DeFries, Willcutt, Pennington, & Olson, 2015, 2016; Willcutt et al., 2007).

Procedure

As described in detail in previous papers, the twins completed an extensive battery of measures of academic achievement, general cognitive ability, neuropsychological functioning, and component reading and language skills during two initial testing sessions at the University of Colorado Boulder. An additional battery of measures of executive functions, psychopathology, and reading comprehension were then administered during a second day of testing at the University of Denver. The battery of measures for the five year longitudinal follow-up assessment includes nearly all of the primary measures from the initial testing with the exception of the measures of math achievement.

Measures

Since the time that the CLDRC was first funded in 1991, one of our primary objectives has been to test the etiology of RD, MD, and other aspects of learning difficulty. As a result, nearly all of the twins who participated in the primary study completed a core battery of measures of word reading, spelling, and math. As the goals of the CLDRC evolved the battery of academic achievement measures was first expanded to include measures of reading comprehension and written language, then expanded again most recently to include measures of nearly all dimensions of academic achievement that were described in the definitions of SLD in DSM-5, ICD-10, and IDEA.

The current battery of academic achievement measures in our primary twin study includes measures of basic and higher-order reading (word reading, reading fluency, reading

comprehension), math (calculations, math fluency, word problems), writing (written motor production, sentence writing production and fluency, and expository writing of longer passages), and spelling (spelling production and recognition), and most of these constructs are assessed by multiple measures. Space constraints only permit a brief description of the individual measures of reading and math that are included in the primary analyses described in this paper, but full descriptions of all measures are provided in our previous publications (e.g., Keenan, Betjemann, & Olson, 2008; McGrath et al., 2011; Shanahan et al., 2006; Willcutt, Pennington, et al., 2010; Willcutt et al., 2005; Willcutt et al., 2013).

Reading achievement.—Word reading was assessed with the Reading Recognition subtest from the *Peabody Individual Achievement Test* (PIAT; Dunn & Markwardt, 1970) and a *Time-Limited Word Reading Measure* developed by our group (R. K. Olson, Wise, Conners, Rack, & Fulker, 1989). Reading fluency was assessed by the *Gray Oral Reading Test, 3rd edition* (GORT-3; Wiederhold & Bryant, 2001) and the Sight Word Efficiency subtest from the *Test of Word Reading Efficiency* (TOWRE; Torgesen, Wagner, & Rashotte, 1999). Reading comprehension measures included the *Qualititative Reading Inventory* (Leslie & Caldwell, 2001), the Passage Comprehension subtest from the *Woodcock-Johnson III Tests of Achievement* (Woodcock, McGrew, & Mather, 2001), and Comprehension scores from the *PIAT and GORT-3*.

Spelling Achievement.—Spelling production was assessed by the Spelling subtest from the *Wide Range Achievement Test, Revised* (Jastak & Wilkinson, 1984), and the PIAT Spelling subtest provided a measure of spelling recognition.

Math achievement.—*The PIAT Math* subtest and *WRAT-R Arithmetic* subtest (Jastak & Wilkinson, 1984) were used to assess math calculations. The *WJ-III Applied Problems* subtest requires the participant to solve word problems that are read aloud by the examiner, and the *WJ-III Math Fluency subtest* is a paper-and-pencil measure that requires the participant to complete as many simple arithmetic problems as possible within a three minute time limit.

Longitudinal outcome measures.—The initial papers based on the longitudinal follow-up component of the CLDRC include a description of the battery of measures of academic and broader developmental outcomes (Wadsworth et al., 2007; Willcutt et al., 2007). As noted earlier, the follow-up battery includes nearly all of the primary measures of academic achievement and functional outcomes that were included in the initial twin study, with the exception of the measures of math achievement that were added to the follow-up battery more recently.

Structure and co-occurrence of SLDs

Covariance between dimensions of academic achievement

Initial confirmatory factor analyses of the most widely-used measures of academic achievement generally support a structural model of academic skills that includes separate but correlated dimensions of reading, writing, and math (e.g., Breaux, 2009; McGrew & Woodcock, 2001; Shrank, McGrew, & Mather, 2014), which may then be subdivided into

more specific components of reading (e.g., single word reading, reading fluency, and reading comprehension), math (e.g., math facts, math calculations, and word problems), and written expression (handwriting production, spelling, grammar, and written composition). This overall structural model of academic achievement also provides the foundation for current definitions of SLD in DSM-5, ICD-10, and IDEA. However, important questions remain regarding the validity of the distinction between different aspects of reading and math and the optimal placement of spelling and writing difficulties in these models.

As a first step to evaluate the structure of academic achievement in our sample, we examined the correlations between composite measures of different components of reading, math, and spelling in the latest CLDRC twin sample (Table 1). Analyses were restricted to the subset of our current sample with data available for all measures of these constructs (N = 510), and measures of writing were not included because the number of participants that also completed the writing measures is still too small for these analyses. Correlations were significant and positive between all measures of academic achievement, clearly illustrating the significant shared variance among different dimensions of learning difficulties. In addition, these results also provide preliminary support for the validity of the distinctions between some aspects of SLDs. Correlations were higher between composite measures of word reading and reading fluency (r = .85) than between either of these measures and measures of reading comprehension (r = .65 - .70) or math (r = .50 - .66). Similarly, correlations between measures of math calculations and math word problems (r = .69) were higher than the correlations between these math measures and the measures of reading and spelling (mean r = .53).

Taken together, these results support a structural model of learning difficulties that includes distinct but correlated dimensions of reading and math within the overarching construct of SLD.). In contrast, the high correlation between composite measures of spelling and word reading replicate extensive previous research that suggests that spelling difficulties may be best conceptualized as a feature of RD rather than a separate SLD or part of WD (for a review see Peterson & Pennington, 2012).

Comorbidity between SLDs in reading and math

Although dimensional analyses of the covariance between individual differences in different aspects of learning are an important starting point, SLDs are explicitly defined by academic achievement that falls below a specified threshold in the lower tail of the population distribution. Therefore, we also completed a series of new analyses for this paper to examine rates of comorbidity between groups with SLDs defined by deficits in different aspects of reading and math, including the measures of math fluency and word problems added to our battery most recently. SLDs in each aspect of reading (word reading, reading fluency, and reading comprehension) and math (math calculations, math fluency, and math word problems) were defined by a cutoff score at the 10th percentile of the estimated population distribution on that measure, and rates of comorbidity were then calculated between each definition of RD and each definition of MD. Results were similar for rates of comorbid RD in groups with MD and rates of comorbid MD in groups with RD. Therefore, for simplicity we report the rates of comorbid MD when probands were selected for RD.

Results revealed significant comorbidity between RD and MD no matter how each group was defined, but also revealed preliminary evidence of differences in the frequency of comorbidity as a function of the different definitions of RD and MD. When RD was defined by a deficit in word reading (N = 70), nearly half of the probands with RD also met criteria for MD as defined by a deficit in math calculations (47%). This rate of comorbidity is very similar to the rate of comorbidity when MD was defined by a deficit in math fluency (50%) or word problems (51%), and is consistent with the results of previous analyses of our entire twin sample (Willcutt et al., 2013).

When RD was defined by a deficit in reading fluency (N = 68), rates of comorbidity were higher when MD was defined by a deficit in math fluency (63%) than by weaknesses in math calculations (47%) or word problems (41%). This stronger association between deficits in fluency may potentially reflect the impact of slow processing speed across different aspects of academic fluency. In contrast, individuals with a deficit in reading comprehension (N = 71) were more likely to have a deficit in math word problems (69%) versus math calculations (49%) or math fluency (38%), potentially due to the importance of language comprehension for these academic skills.

These results should be interpreted with caution because the number of participants with significant weaknesses in math fluency and word problems is still relatively small. Nonetheless, these preliminary findings suggest that the frequency and implications of comorbidity between RD and MD may potentially differ as a function of the specific aspects of reading or math difficulties that are used to define each SLD.

Etiology of SLDs in reading and math

Twin studies compare pairs of identical (monozygotic, or MZ) versus fraternal (dizygotic, or DZ) twins to estimate the relative importance of genetic and environmental influences on individual differences or group deficits in a trait. Twin studies of unselected samples consistently indicate that genetic influences contribute to individual differences in reading and math and their covariance (e.g., Hart et al., 2010). However, categorical SLDs and most other complex cognitive and behavioral disorders are defined by a diagnostic threshold imposed upon a quantitative measure that is continuously distributed in the population (e.g., Coghill & Sonuga-Barke, 2012; Willcutt, Pennington, & DeFries, 2000). Therefore, as part of the initial work that eventually led to the initiation of the CLDRC, DeFries and Fulker developed a powerful and versatile multiple regression method to test the etiology of the extreme scores that define SLDs (DeFries & Fulker, 1985, 1988).

Univariate multiple regression analyses of selected twin samples

DeFries-Fulker (DF) analysis is based on the differential regression of MZ versus DZ cotwin scores toward the population mean when probands are selected due to a deficit on a continuously distributed measure like academic achievement. Although scores of both MZ and DZ cotwins are expected to regress toward the population mean, scores of DZ co-twins should regress further than scores of MZ cotwins to the extent that the proband deficit is influenced by genes. After appropriate standardization and transformation of scores, DF analysis provides a direct estimate of the heritability of the group deficit on the selected

measure (h^2_g), along with estimates of shared (c^2_g) and nonshared (e^2_g) environmental influences. Shared environmental influences (c^2_g) are environmental factors that increase the similarity of individuals within a family in comparison to unrelated individuals in the population. In contrast, *nonshared environmental influences* (e^2_g) affect only one member of a twin pair or affect the two twins independently (e.g., a head injury that happens by chance to one of the twins), leading to random environmental influences for members of twin pairs.

Univariate DF multiple regression models were used to test the etiology of group deficits on each of the measures of reading and math in our latest sample. For each measure probands were once again selected due to scores below the 10th percentile in the estimated population distribution, yielding mean MZ and DZ proband scores that fell 1.6 – 1.8 standard deviations below the estimated population mean (Table 2). The mean of the MZ cotwins regressed significantly less toward the population mean than the mean of the DZ cotwins for all measures of reading and math, indicating that deficits on each of these measures are significantly heritable. Results of the full regression models yielded point estimates for heritability that ranged from .62 - .77, indicating that genetic influences account for 62 – 77% of the proband deficit on each measure of reading or math difficulties. Shared environmental influences accounted for 4 – 20% of the proband deficit in each domain, and 11 – 20% of each weakness was due to nonshared environmental influences or measurement error.

Bivariate analyses of the etiology of comorbidity between RD and MD

Over a dozen different hypotheses have been proposed as competing explanations for the comorbidity between developmental disorders, including the possibility that shared genetic or environmental risk factors may increase risk for multiple disorders (e.g., Neale & Kendler, 1995; Rhee, Hewitt, Corley, Willcutt, & Pennington, 2005). One of the most prominent models is the “generalist genes” hypothesis advanced by Plomin and colleagues (e.g., Kovas, Harlaar, Petrill, & Plomin, 2005; Kovas et al., 2007). This model proposes that the high comorbidity between RD and MD may reflect domain general genetic influences that increase risk for RD, MD, and potentially other learning difficulties. In this model these shared genetic risk factors then act in combination with additional genetic or environmental influences that are uniquely associated with each disorder.

A straightforward adaptation of the DF multiple regression approach can be used to estimate the extent to which comorbidity between RD and MD is due to genetic or environmental influences that increase risk for both disorders. Rather than testing for the differential regression of MZ and DZ cotwin scores on the measure that was used to select the probands, a bivariate extension of the DF model compares cotwin scores on the measure of the unselected disorder (e.g., cotwin math scores when probands are selected due to reading difficulties). The full bivariate regression model then provides an estimate of *bivariate h2g*, an index of the extent to which the proband deficit on the selected measure is due to genetic influences that are also associated with deficits on the unselected measure (e.g., Light & DeFries, 1995). The estimates of univariate and bivariate h^2_g can then be used to estimate the *genetic correlation* between extreme scores on the two measures ($r_{g[SEL]}$). The genetic correlation indicates the extent to which the genetic influences on either RD or MD are also

associated with the other disorder (e.g., Gayan & Olson, 2001). A genetic correlation of zero would indicate that none of the same genetic influences contribute to both RD and MD, where as genetic correlation of 1.0 would indicate that all of the genetic influences on either RD or MD also increase risk for the other disorder.

Table 3 summarizes the genetic correlations between deficits in the different aspects of reading and math assessed in our sample. Genetic correlations were extremely high between the three measures of reading ($r_{g[sel]}$ = .77 - .91), suggesting that most genetic influences on reading are general effects that lead to weaknesses in all aspects of reading. In contrast, genetic correlations between math measures were somewhat more modest ($r_{g[sel]}$ = .38 - .66), suggesting that both general and specific genetic influences increase risk for different aspects of math.

In terms of comorbidity, genetic correlations were significant and at least moderate in magnitude for all measures of reading and math, with the highest genetic correlations observed between measures of reading and math fluency ($r_{g[sel]}$ = .69 - .79). These results suggest that the pervasive comorbidity between RD and MD is due at least partially to shared genetic influences, and these shared genes may be especially important for deficits in academic fluency.

Functional outcomes of RD and MD

A final series of new analyses examined the impact of RD, MD, and their comorbidity on developmental outcomes in and outside of school. Earlier cross-sectional analyses in our sample indicated that both RD and MD are associated with significant impairment on virtually all measures of “real world” academic functioning, along with greater social difficulties and higher levels of ADHD symptoms and many aspects of internalizing and externalizing psychopathology (e.g., Willcutt et al., 2013). Further, these difficulties were often most severe in the subgroup with both RD and MD, underscoring the potential impact of comorbidity on the developmental outcomes of SLDs.

In this section we extend these initial results in new longitudinal analyses of the five-year outcomes of groups of individuals that met criteria for RD only (N = 57), MD only (N = 36), RD+MD (N = 60), or neither disorder (N = 81) based on their scores on measures of word reading and math calculations at the initial assessment. While the comorbid group had slightly more severe deficits in both reading and math than the groups with RD or MD only (d = .25 - .40), all of the results described in this section remained significant when these differences were controlled.

Academic outcomes

Nearly two-thirds of the individuals who met criteria for RD at time 1 continued to meet criteria for RD at the follow-up assessment (Figure 1), but RD was significantly more stable among individuals who also met criteria for MD at time 1 (it is not yet possible to test the stability of MD because math achievement measures were only recently added to our longitudinal follow-up battery). Similarly, while both RD and MD at the initial assessment were independently associated with a range of negative academic outcomes, twins with both

disorders were most likely to report ongoing reading difficulties and to have been retained or received special education services in school (Figure 1).

Psychopathology outcomes

In comparison to the group without an SLD, individuals with RD only, MD only, or both RD and MD were significantly more likely to meet criteria for ADHD and conduct disorder five years later (Figure 2), but the rate of ADHD was significantly higher in the group with both RD and MD than the groups with MD or RD alone. Similarly, only the comorbid group exhibited a higher rate of depression than the comparison group at the follow-up assessment, and no other group comparisons were significant. Individuals with MD at the initial assessment were more likely than individuals in the control group to report that they regularly consumed alcohol or used cannabis five years later, whereas initial RD status was not independently associated with these substance use outcomes.

Conclusions and Future Directions of the CLDRC

The structure of SLDs

Correlations are medium to large in magnitude between all dimensions of math and reading, and 40 – 60% of individuals with RD or MD also meet criteria for the other disorder. On the other hand, correlations between all dimensions of SLD are significantly less than unity, and nearly half of all individuals with RD or MD do not meet criteria for the other SLD. Taken together, these results provide initial support for a structural model of learning difficulties that includes distinct but correlated dimensions of academic difficulties within the overarching construct of SLD. However, the current results and our other recent analyses also underscore some important weaknesses in these models. For example, the high correlation between word reading and spelling ($r = .85$) replicates previous research that suggests that spelling difficulties may be best conceptualized as a feature of RD rather than a separate SLD or part of WD (for a review see Peterson & Pennington, 2012).

The initial battery of academic achievement measures in the CLDRC twin study assessed multiple dimensions of academic achievement, and often included multiple measures of each academic construct. However, despite our extensive test battery several constructs were only assessed by a single measure, and some important aspects of academic functioning were not assessed until recently. The preliminary analyses of math fluency and word problems for this paper illustrate our ongoing efforts to fill important gaps in our battery of academic achievement measures, and we have also recently expanded our battery of writing measures. After the sample with these new measures becomes sufficiently large over the next several years, we will be able to test comprehensive models of the structure of SLDs using state-of-the-art structural equation models with latent traits based on multiple measures of all putative dimensions of learning difficulties included in DSM-5, ICD-10, or other models.

Developmental stability and outcomes of SLDs

The current longitudinal analyses add to a growing literature that suggests that deficits in word reading are highly stable (Wadsworth et al., 2007; Willcutt et al., 2007). Further, our results clearly indicate that both RD and MD are associated with a range of negative

outcomes, with the worst outcomes often occurring for individuals with both disorders. In contrast, little is known about the stability of deficits in other aspects of reading, math, or writing or the long-term consequences that may result from these difficulties.

To address these gaps in the literature, we recently expanded the assessment battery for the longitudinal follow-up component of the CLDRC twin study. These new measures will eventually allow our Center to test the stability and functional outcomes of all aspects of RD, MD, WD, and their comorbidity, including novel analyses of developmental outcomes in emerging and early adulthood. These analyses of longer-term outcomes will provide important information about the developmental course and prognosis of SLDs, including aspects of impairment that may only become relevant later in development. For example, early difficulties in writing might predict greater academic impairment later in development due to the increased writing demands that students encounter in high school and postsecondary education.

Etiology

Although the current results should be interpreted with caution due to the small number of probands for some measures, our findings provide additional evidence that deficits in all aspects of reading and math are significantly heritable. Further, the ubiquitous comorbidity between RD and MD is primarily explained by shared genetic influences that increase risk for multiple SLDs. As our sample size increases over the next several years it will become feasible to test the etiology of deficits on all specific dimensions of RD, WD, MD, along with the frequent co-occurrence between different SLDs and between each SLD and other disorders such as ADHD and other developmental psychopathologies. These behavioral genetic results will then help to identify the specific measures that may be most useful for inclusion in the ongoing and new molecular genetic studies in our Center, providing a unique opportunity to identify the shared and unique genetic and environmental influences that increase risk for SLDs and related disorders.

Neuropsychological and neuroimaging approaches

A final overarching objective of the CLDRC involves the use of neuropsychological and neuroimaging methods to understand the complex etiology and neurobiology of SLDs and other developmental disorders. In contrast to early theoretical models that proposed that a single neuropsychological deficit was a necessary and sufficient cause of complex disorders such as RD and MD, we have proposed multiple deficit neuropsychological models that explicitly hypothesize that SLDs and others complex dimensions and disorders arise from the combined effects of multiple neuropsychological weaknesses (McGrath et al., 2011; Pennington, 2006; Peterson et al., 2017; Willcutt, Betjemann, et al., 2010). If these multiple deficit models are correct they may provide a compelling theoretical framework to understand the underlying mechanisms of the comorbidity between different aspects of SLD, as it is plausible that some neuropsychological weaknesses may be general risk factors that are associated with multiple dimensions of SLD, whereas other processes may be uniquely associated with specific weaknesses in reading, math, or writing.

Neuropsychological analyses in the CLDRC have shown that groups with RD, MD, and ADHD exhibit significant weaknesses on most of the neuropsychological measures in our battery (e.g., Peterson et al., 2017; Willcutt, Betjemann, et al., 2010; Willcutt et al., 2013). These results support the multiple deficit hypothesis and suggest that rather than qualitatively distinct neuropsychological weaknesses, SLDs and other related disorders may be distinguished by quantitative differences in the specific profile or severity of neuropsychological weaknesses across multiple domains that are impaired to some extent in most or all disorders. For example, while weakness in phonological processing is clearly the strongest neuropsychological correlate of reading difficulties in our sample and the overall literature (e.g., Wagner, 1986; Willcutt et al., 2013), not all children with RD have phonological weaknesses (Pennington et al., 2012), and RD is also independently associated with weaknesses in verbal reasoning, naming speed, and processing speed. Similarly, MD is associated with weaknesses in phonological processing, executive functions, verbal reasoning, and processing speed in our sample, and other studies suggest that math difficulties may be uniquely associated with weaknesses in number sense, the foundational understanding of conceptual aspects of numbers such as quantities and comparisons of magnitude (e.g., Geary, 1993; Iuculano, Tang, Hall, & Butterworth, 2008).

In terms of comorbidity, our results suggest that cognitive processing speed is one plausible candidate for a domain-general cognitive factor that may account for shared variance and comorbidity among reading, math, and other disorders such as ADHD (McGrath et al., 2011; Peterson et al., 2017; Shanahan et al., 2006; Willcutt, Betjemann, et al., 2010; Willcutt et al., 2005). Over the next several years we will continue to administer our extensive battery of neuropsychological measures to additional participants in our twin study. This larger sample will allow us to test which neuropsychological deficits may be shared weaknesses across all aspects of SLDs, and which may be uniquely associated with specific aspects of learning difficulties.

Finally, we recently initiated a new structural and functional neuroimaging study that will include a subsample of CLDRC participants with RD only, MD only, both RD and MD, and neither disorder, yielding the largest sample to date for a neuroimaging study of RD and MD. This study will allow us to test for the first time which neural markers are uniquely associated with reading and math, and which neural correlates may help to explain the shared variance that underlies comorbidity between RD and MD.

Conclusion

The overarching long-term objective of the CLDRC is the development of a comprehensive etiological and neurobiological model of SLDs to optimize the classification, diagnosis, and treatment of learning disabilities and related disorders. This is a daunting challenge that requires the successful integration of diverse literatures, scientific approaches, and analytic strategies, and it cannot be accomplished by a single scientist or research lab working in isolation. By facilitating synergistic collaborations between researchers with diverse and complementary areas of expertise, The *Eunice Kennedy Shriver* NICHD Learning Disability Research Centers and Hubs provide critical support for the synergistic interdisciplinary research approaches that will be essential for the next generation of studies of SLDs.

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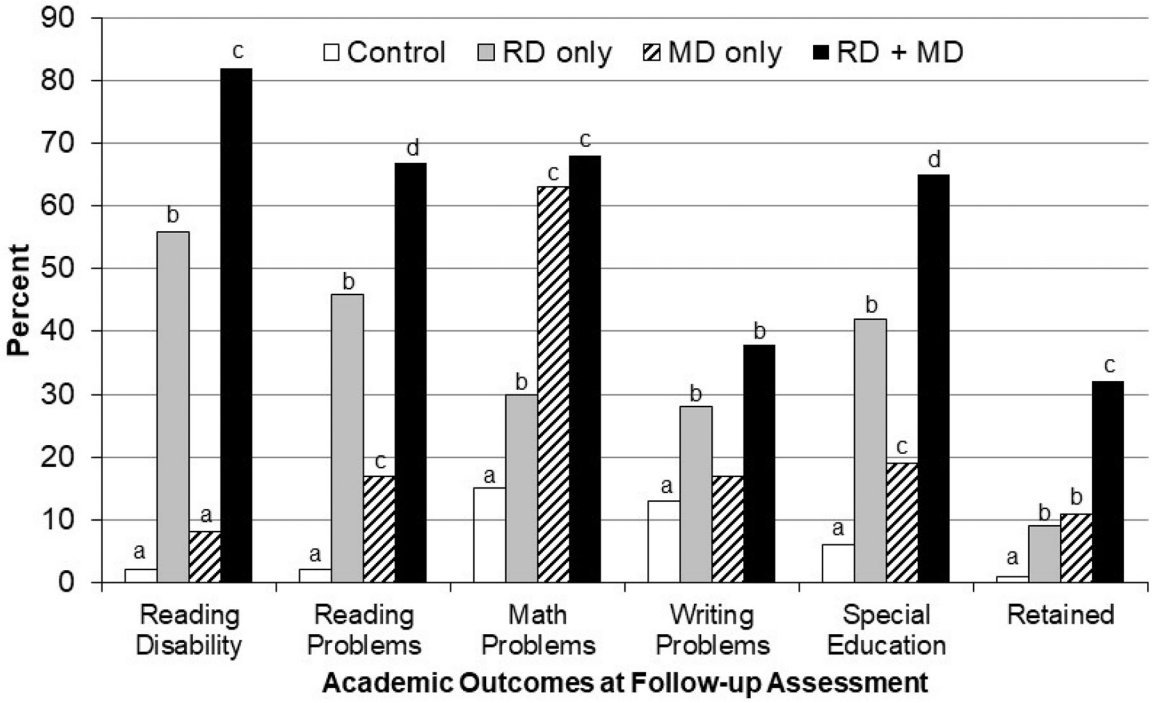

Figure 1.

Academic outcomes of groups with and without RD and MD at the initial assessment. Bars with different subscripts are significantly different ($P < .05$).

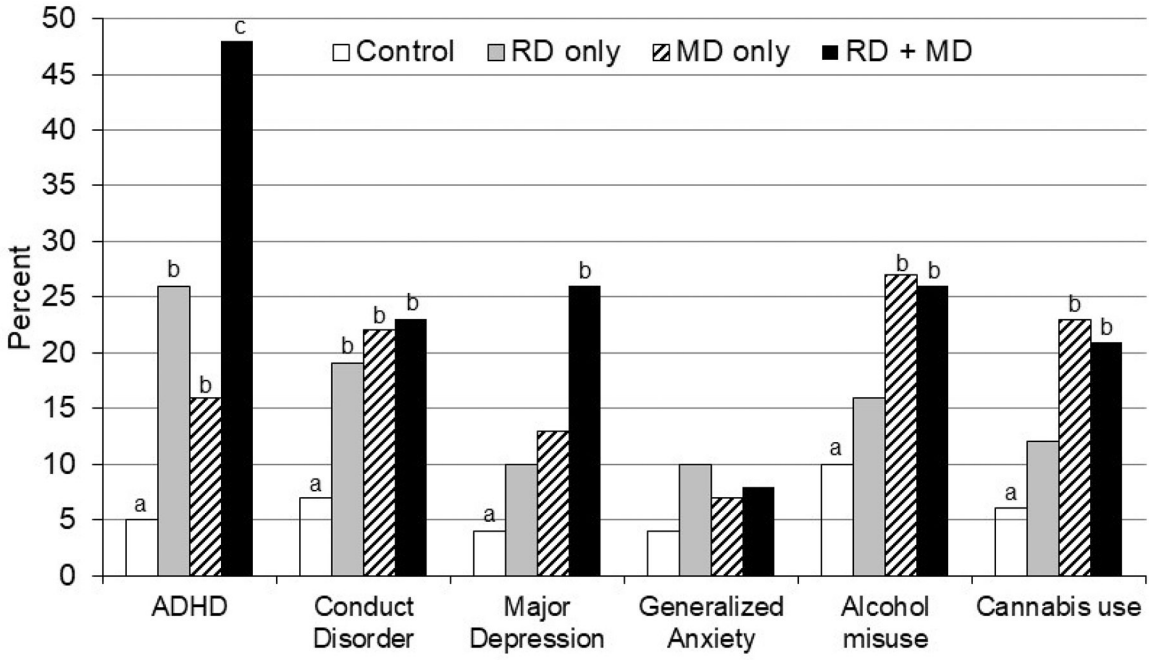

Figure 2.

Psychopathology and substance use outcomes in groups with and without RD and MD at the initial assessment. Bars with different subscripts are significantly different ($P < .05$).

Table 1

Phenotypic correlations between composite measures of reading, math, and spelling

	Word Reading	Reading Fluency	Reading Comp.	Math Calculation	Math Fluency	Word Problems
Reading Fluency	.85	--				
Reading Comprehension	.70	.65	--			
Math Calculation	.59	.58	.51	--		
Math Fluency	.50	.66	.35	.62	--	
Word Problems	.51	.50	.60	.69	.52	--
Spelling	.85	.74	.55	.55	.49	.51

N = 510. All correlations are significant (P < .001).

Table 2

Multiple regression analyses of group deficits in reading and math

	MZ pairs[a]			DZ pairs[a]			
		Proband	Co-twin		Proband	Co-twin	
	N[b]	M (SD)	M (SD)	N[b]	M (SD)	M (SD)	h^2_g (SE)
Reading							
Word Reading	340	−1.64 (0.52)	−1.48 (0.62)	278	−1.61 (0.49)	−0.92 (0.90)	0.65 (0.07)***
Reading Fluency	108	−1.62 (0.45)	−1.39 (0.81)	103	−1.61 (0.47)	−0.80 (1.21)	0.72 (0.11)***
Reading Comprehension	88	−1.77 (0.71)	−1.57 (0.82)	90	−1.71 (0.74)	−0.86 (1.09)	0.77 (0.13)***
Math							
Calculations	274	−1.59 (0.47)	−1.30 (0.71)	225	−1.58 (0.54)	−0.80 (0.88)	0.62 (0.08)***
Math Fluency	28	−1.67 (0.49)	−1.29 (0.71)	29	−1.67 (0.53)	−0.68 (0.99)	0.73 (0.29)**
Word Problems	29	−1.69 (0.49)	−1.38 (0.79)	30	−1.81 (0.69)	−0.87 (1.16)	0.67 (0.29)*

Note.

*= P < .05,

**= P < .01,

***P < .001.

[a]Scores are expressed as standard deviations from the estimated population mean.

[b]Total number of pairs in which at least one twin met the criteria for the proband group.

Table 3

Genetic correlations between group deficits on different dimensions of reading and math

Variable 1	Variable 2					
	Word Reading	**Reading Fluency**	**Reading Comp.**	**Math Calculation**	**Math Fluency**	**Word Problems**
Word Reading	--					
Reading Fluency	.90 / .91	--				
Reading Comprehension	.88 / .88	.84 / .77	--			
Calculations	.53 / .61	.61 / .45	.51 / .58	--		
Math Fluency	.46 / .28	.71 / .79	.38 / .24	.61 / .66	--	
Word Problems	.54 / .44	.48 / .29	.43 / .53	.51 / .55	.38 / .48	--

Note: The first value for each pair of variables indicates the genetic correlation when probands were selected for variable 1, and the second value indicates the genetic correlation when probands were selected for variable 2.