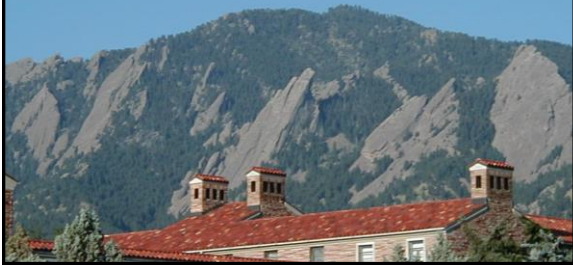


Understanding “the whirling ball of comorbidity”: Reading Disability, Math Disability, and ADHD

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Overview

- What is comorbidity and why does it matter?
- Why does comorbidity matter?
- What causes comorbidity between reading disability, math disability, and ADHD?
- What are the implications of comorbidity for assessment and treatment?
- Gaps in the literature and suggestions for the future

Our Samples most relevant to comorbidity

- Colorado Learning Disabilities Research Center
 - School-based screening of 8-18 year old twins
 - Reading or math difficulty: 426 identical twin pairs and 722 fraternal pairs
 - ADHD: 149 MZ twin pairs and 341 DZ twin pairs
 - Comparison: 347 MZ pairs, 430 DZ pairs
- International Longitudinal Twin Study of Early Reading
 - Unselected sample of 928 twins in Colorado
 - First tested prior to kindergarten, now completing 9th grade follow-up
 - Parallel studies in Australia, Norway, and Sweden
- Community Studies of ADHD and reading difficulties
 - Unselected sample enriched for lower SES schools; 7-13 years old
 - 8,250 screened to identify 750 ADHD and 600 RD cases
 - Feeder for targeted studies of RD and ADHD in diverse populations
- Colorado Study of ADHD in College Students
 - 3,913 Psychology 1001 students screened
 - 350 completed individual testing
 - 70 completed fMRI

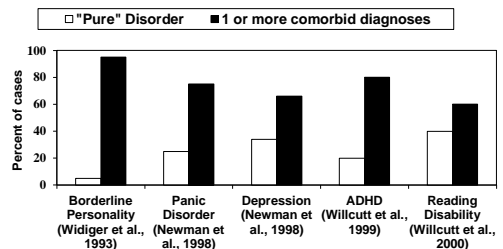
Key Measures

- Reading
 - Single word reading (PIAT, WJ-III)
 - Reading fluency (WJ-III, TOWRE)
 - Reading comprehension (subset of cases)
- Math
 - Math calculations (WJ-III, WRAT, PIAT)
 - Math fluency (subset; WJ-III)
 - Word problems (subset of cases; WJ-III)
- ADHD
 - Parent and teacher ratings scales (DBRS or SWAN)
 - Parent interview (DICA-IV or DISC-IV)
- Neuropsychological functioning
 - Response inhibition (stop-signal, continuous performance test)
 - Working memory (WISC, span tasks)
 - Processing speed (WISC, experimental measures)
 - Response consistency / variability
 - Phonological processing

Definitions for this talk

- Reading Disability: Below the 10th percentile of the population on a test of single-word decoding (PIAT or WJ-III).
- Math Disability: Below the 10th percentile of the population on a test of math calculations (PIAT or WJ-III).
- ADHD
 - Full criteria for DSM-IV ADHD
 - Parent interview (DICA-IV) and teacher ratings (DSM-IV)
 - DSM-IV subtypes collapsed.

Comorbidity is the rule, not the exception

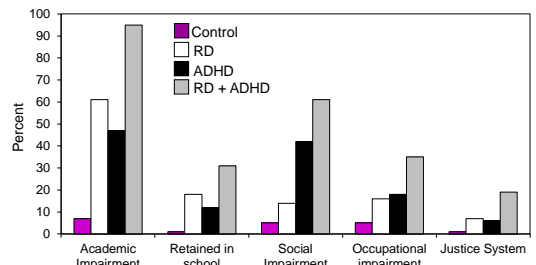


Why should we care about comorbidity?

- Comorbidity is ubiquitous
 - 25 - 35% co-occurrence of RD and ADHD
 - 40 - 60% co-occurrence of RD and MD
- Diagnostic uncertainty has key treatment implications
 - RD → ADHD
 - ADHD → RD
 - Shared risk factor → RD + ADHD
- Negative outcomes
 - increased frequency, severity of associated difficulties
- Comorbidity challenges causal models that assume:
 - Disorders are categorical and discrete.
 - Each disorder has a unique necessary and sufficient cause.

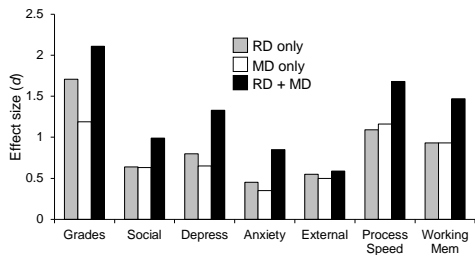
Implications of Comorbidity: Impairment in groups with RD, ADHD, and RD+ADHD

(Willcutt et al., 2007, 2010; Willcutt, Petrill et al., 2013)

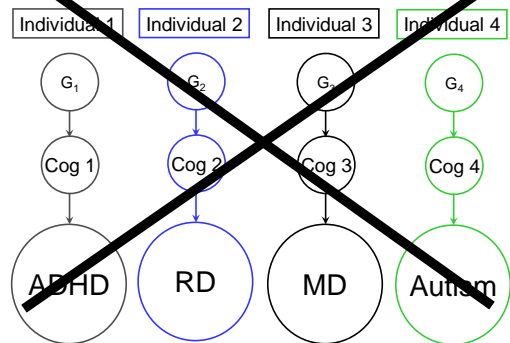


Implications of Comorbidity: Groups with RD, MD, and RD+MD

(Willcutt, Petrill, et al., 2013)



The OGOD model One Gene, One Deficit, One Disorder

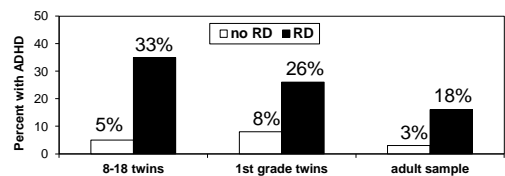


Competing Explanations for Comorbidity

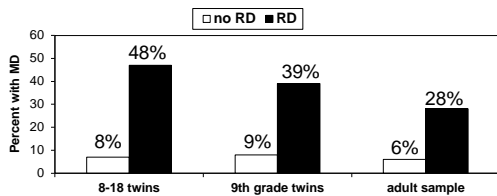
(e.g., Caron & Rutter, 1991; Neale & Kendler, 1995; Rhee et al., 2005)

- Clinical Sample Bias:** Comorbidity is only present in clinical samples.
- Method bias:** Comorbidity occurs only because both disorders are assessed with the same measure.
- Rater bias:** raters are more likely to endorse symptoms of a second disorder if the child has the first disorder.
- Secondary symptom (phenocopy) hypothesis:** Disorder #1 causes an individual to exhibit the symptoms of disorder #2 when they do not actually have the disorder.
- Causal Hypothesis:** Disorder #1 directly causes disorder #2.
- Common Etiology Hypothesis:** The two disorders co-occur due to shared risk factors.

Rate of ADHD in groups with and without RD in our community samples



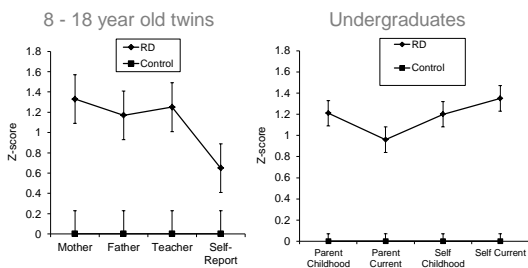
Rate of Math Disorder in groups with and without RD in our community samples



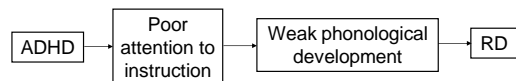
Correlations between reading and math achievement test scores and reading and math grades

	Reading Achievement Test	Reading Grades
Math Achievement Test	.56	.36
Math grades	.37	.51

Attention Problems in Individuals With and Without RD (Willcutt, Chhabildas, & Pennington, 1998; Willcutt et al., under review)



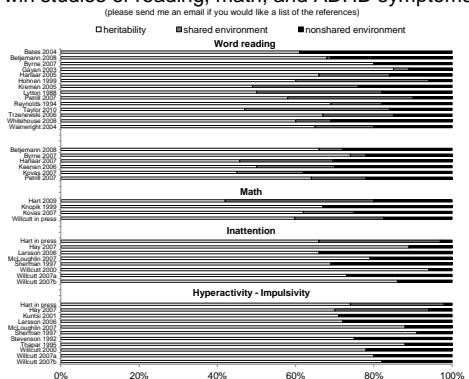
One plausible causal model

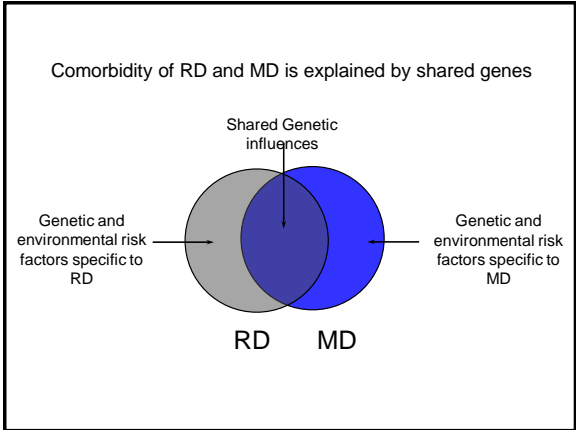
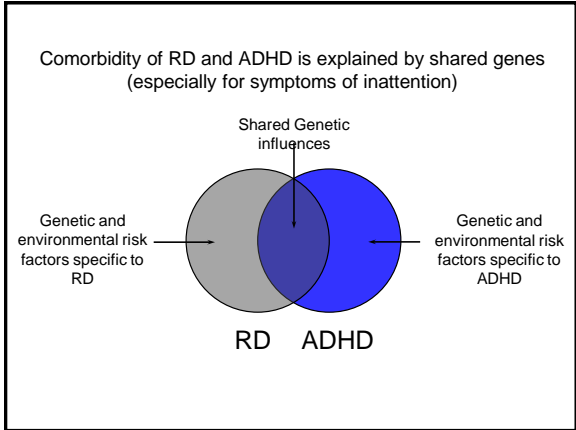


Causes of RD and ADHD

- Family studies
 - RD, MD, and ADHD are each significantly familial
 - RD, MD, and ADHD run in the same families
 - So it's genetic, right?
- Twin Studies: disentangle three causes of individual differences in reading or ADHD
 - Heritability: the extent to which the disorder is due to genetic influences
 - Shared environment: the extent to which the disorder is due to environmental factors that affect both twins in a similar way.
 - Nonshared environment: the extent to which the disorder is due to environmental factors that are specific to the child with the disorder.

Twin studies of reading, math, and ADHD symptoms





Tests of the Competing Hypotheses

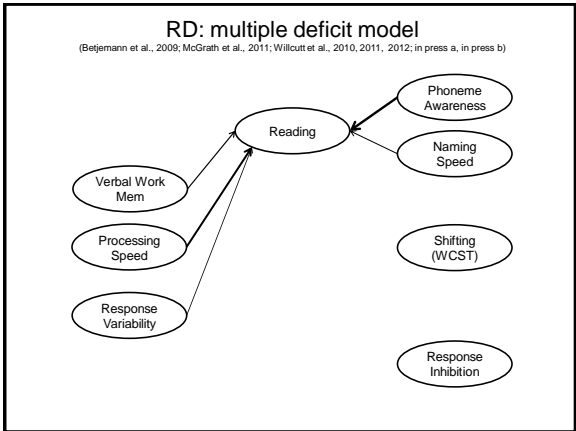
Artifactual Hypothesis	Result
Clinical Sample Bias	Not supported
Method Bias	Not supported
Rater Bias	Not supported
Secondary Symptom	Not supported

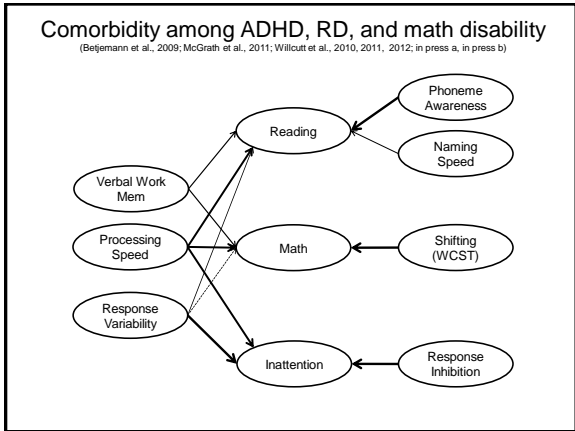
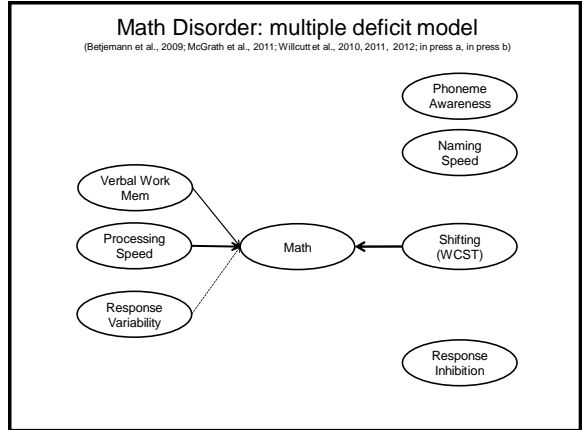
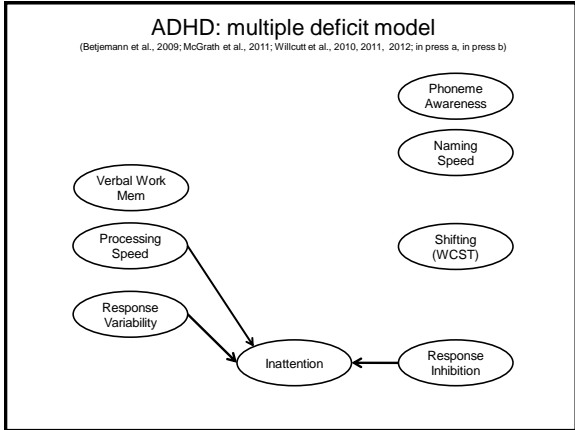
"True Comorbidity" Models

Causal Hypothesis	Come back next year!
Common Etiology	Supported: Shared genetic risk factors

- Surprises from molecular genetic studies of ADHD**
(e.g., Gizer et al., 2009)
- 30+ candidate genes significant in at least one study
 - Odds ratios: 1.05 - 1.23
 - Total variance explained: 3 - 5%
 - The story is similar for genome-wide association studies and other approaches and for virtually RD, MD, and virtually all other complex disorders
 - Very small effect sizes
 - Additive and interactive effects of many genes acting together

- Neuropsychological Measures**
(send me an email if interested in specific tasks)
- **Reading component processes**
 - Phonological awareness: detect and manipulate phonemic constituents of speech
 - **Executive functions**
 - Inhibition: suppress a prepotent response when it is incorrect
 - Working memory: retain and manipulate information in memory
 - Shifting: flexibly shift cognitive set
 - **Processing efficiency**
 - Processing speed: motor responses
 - Naming speed: rapidly name letters, colors, numbers, objects
 - Response variability: intraindividual variability in reaction time
 - **Key missing domains**
 - Delay aversion / delay of gratification
 - Numerosity / number-sense





- ### Conclusions and Future Directions of our Group
- RD, MD, and ADHD are frequently comorbid
 - Future: longitudinal models; academic fluency and comprehension
 - Comorbidity is associated with multiple negative outcomes
 - Future: additional adult outcomes
 - RD, MD, and ADHD are influenced by multiple genes, none of which is a necessary or sufficient cause
 - Shared genetic influences lead to comorbidity between RD, MD, and ADHD
 - Future: What are these genes, what is their function, and how do they interact?
 - These common genes may lead to slow processing speed or working memory difficulties.
 - Future: brain imaging and neurophysiology

- ### Clinical and Educational Implications
- When assessing RD, MD, or ADHD, clinicians should also screen carefully for the other disorder
 - Colorado Learning Difficulties Questionnaire (Willcutt et al., 2011)
 - Brief ADHD screeners: Barkley, Conners, DuPaul, SNAP
 - When RD, MD, and ADHD do co-occur, each disorder is likely to require treatment
 - More work is needed
 - What are the implications for educational interventions in school?
 - Does comorbidity matter for treatment outcome?
 - We hope that genetic and neuropsychological approaches will eventually facilitate diagnosis, but "it's all very complicated"...