

A Genetic Study of Attention Deficit Hyperactivity Disorder, Conduct Disorder, Oppositional Defiant Disorder and Reading Disability: Aetiological overlaps and implications

Neilson C. Martin^{a*}, Florence Levy^b, Jan Pieka and David A. Hay^a

^a*Curtin University of Technology, Australia;* ^b*Prince of Wales Hospital and University of New South Wales, Australia*

Attention Deficit Hyperactivity Disorder (ADHD) commonly co-occurs with Oppositional Defiant Disorder, Conduct Disorder and Reading Disability. Twin studies are an important approach to understanding and modelling potential causes of such comorbidity. Univariate and bivariate genetic models were fitted to maternal report data from 2040 families of twins from the Australian Twin ADHD Project. All measures showed a heritability of over 0.8 and little role for the common family environment, except for the combined subtype of ADHD with a heritability of 0.69 and a common environment of 0.19. About one-third of the genetic variance in ADHD was shared with the other behaviours, the largest overlap being with Oppositional Defiant Disorder. Common environmental effects were shared between the combined ADHD subtype and the other measures. Some implications of these findings for home and school are discussed.

Keywords: Attention Deficit Hyperactivity Disorder; Comorbidity; Conduct Disorder; Oppositional Defiant Disorder; Reading disability; Twins

Introduction

Attention Deficit Hyperactivity Disorder (ADHD) has been shown to be a highly heritable disorder utilising twin studies (Martin, Scourfield, & McGuffin, 2002) and

*Corresponding author. School of Psychology, Curtin University of Technology, GPO Box U1987, Perth, WA 6845, Australia. Email: n.martin@curtin.edu.au

family studies (Biederman, Faraone, Keenan, Knee, & Tsuang, 1990). The prevalence of ADHD is in the region of 5–10% in the general population (Milberger, Faraone, Biederman, Testa, & Tsuang, 1996), but family studies have found that 30–35% of full siblings of affected children also meet ADHD criteria (Faraone, Biederman, & Friedman, 2000). In the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV) (American Psychiatric Association [APA], 1994) ADHD is diagnostically separated into three subtypes; namely, Predominantly Inattentive (ADHD-I), Hyperactive/Impulsive (ADHD-HI), and Combined (ADHD-C).

ADHD very often occurs comorbidly with other disorders such as Oppositional Defiant Disorder (ODD), Conduct Disorder (CD) and Reading Disability (RD) (Levy, Hay, Bennett, & McStephen, 2005; Scourfield, Van den Bree, Martin, & McGuffin, 2004). Indeed the European classification (Taylor et al., 2004), which uses the term “hyperkinesis” and requires symptoms of inattention, hyperactivity, and impulsivity, specifically makes the distinction of hyperkinesis with and without CD. The mechanisms by which these comorbidities are mediated are not well known but they are under investigation. The overlap between ADHD, ODD, and other disorders has been explored using latent class analysis (Neuman et al., 2001). These authors found distinct classes with and without comorbidity, suggesting that the comorbid disorder may be genetically distinct from either ADHD or ODD. Further work (Volk, Neuman, & Todd, 2005) suggests that ODD is most commonly found comorbid with the ADHD-C subtype while CD is found with all subtypes. While there are gender differences in ODD and CD in the general population, Levy et al. (2005) found they were much reduced among females and males in the three DSM-IV subtypes.

The overlap of the inheritance components of the disorders is an obvious area to explore, and several such studies have found shared genetic and environmental influences of ADHD with ODD and/or CD (Thapar, Harrington, & McGuffin, 2001; Waldman, Rhee, Levy, & Hay, 2001). Waldman et al. found an almost complete genetic overlap of ADHD with ODD, but more genetic specificity when it came to analysing the overlap of ADHD and CD. This is particularly interesting, given that ODD has sometimes been seen as the developmental precursor of CD.

Genetic methods offer exciting possibilities to understand the relationship of ADHD to reading. The main studies of reading disability in twins have been conducted over more than a decade in Colorado, focusing initially on twins identified with reading problems through the school system. Genetic deficits in phonological awareness have been found to underlie problems with phonological decoding and word reading (Gayan & Olson, 2001). A slightly different approach was used by Bates et al. (2004), who specifically assessed the genetics of the dual route model of reading, as well as lexical and sublexical routes to spelling.

There have been different approaches to the genetics of the relationship of ADHD to reading. The twin approach has been used by the Colorado group (Willcutt, Pennington, & DeFries, 2000) and also by Stevenson (2001), who went further and identified a closer relationship of reading to inattention than to hyperactivity/impulsivity. Molecular approaches to ADHD, reading, and their overlap are summarised in Levy, Hay, and Bennett (2006). One of the genes on chromosome 6

that has been repeatedly implicated in reading has been found to be pleiotropic, in that it also influences ADHD (Willcutt et al., 2002). In a genome-wide scan of ADHD, at least three genes turned out to be pleiotropic for both behaviours (Loo et al., 2004).

The aim of the current study was to take questionnaire measures for ADHD, CD, RD, and ODD and look for a shared genetic heritability using quantitative genetic methodology in a very large twin sample. While this methodology is powerful, it does require extremely large sample sizes (Neale & Cardon, 1992), which in turn may restrict the approach used to obtain information. Questionnaires rather than face-to-face assessment may be the only affordable means of obtaining such information. This approach can answer the question of why the disorders co-occur so commonly and tease apart the genetic influences from the environmental effects acting upon the disorders to better understand how they come about. By looking at the comorbid disorder we can examine whether it is a general link between ADHD and the other disorders or whether particular ADHD subtypes are linked more strongly with particular other disorders. Specific patterns of comorbidities may point to particular aetiological pathways that can then be explored more fully. For example, is the connection between ADHD and ODD/CD biological, or nothing more than children who cannot attend or do well in school becoming frustrated? Similarly, is the connection between ADHD and reading because children who cannot attend fail to develop appropriate reading skills, or conversely because children who cannot read become bored—or does it result from a common environmental and/or biological basis to both?

Method

Participants

The participants consisted of 2,040 families of twins from the Australian Twin ADHD Project summarised in Levy, Hay, Waldman, and McStephen (2001). Families were ascertained from the Australian Twin Registry (<http://www.twins.org.au>), a nation-wide, volunteer-based database of twins and higher-order multiple birth families born in Australia. The twin pairs were aged 5–16 years ($M = 13.4$ years, $SD = 3.6$). There were 907 monozygotic (MZ) pairs (456 male, 451 female), 608 same-sex dizygotic (DZ) pairs (317 male, 291 female), 498 male/female DZ pairs, and 27 pairs for whom zygosity could not be assigned (they were excluded from further analyses and are not included in the following counts). In total, 2,044 males and 1,982 females participated.

Each family was sent a questionnaire package for returning by pre-paid mail. The project was approved by Curtin University Human Research Ethics Committee and by the Australian Twin Registry.

Measures

Reading Disability questionnaire. A seven-item questionnaire with high reliability and validity was used to assess RD symptoms (Willcutt, Boada, Pennington, & Riddle, in

press). It contains items such as “Does this child have difficulty with spelling” and “Does this child read below grade or expectancy level”. The responses range from “Not at all” (scored as 0) to “Very much/very often” (scored as 3). Scores are totalled and those scoring more than 1.5 standard deviations below the mean are considered affected.

Australian Twin Behaviour Rating Scale. ADHD symptoms were assessed using the Australian Twin Behaviour Rating Scale (ATBRS) (Levy & Hay, 2001; Levy et al., 2001), a parent-report questionnaire containing 18 items assessing DSM-IV criteria for ADHD as observed in the child over the previous 12 months. It contains items such as “Has difficulty keeping attention on work or games” and “Has difficulty organising tasks or activities”, which follow the language of the diagnostic items in DSM-IV. As with the RD questionnaire, responses ranged from 0 to 3. The scores are then used to define whether each child is affected and with which subtype (inattentive, hyperactive/impulsive, or combined).

The ATBRS also contains 17 items for CD and eight items for ODD, which, as with the ADHD items, are based on the language of the DSM-IV diagnostic criteria and are scored in a similar fashion.

Zygoty questionnaire. Zygoty was assigned using the following process. First the parents were asked whether there had been DNA testing to determine zygoty. If they answered no, then a twin similarity questionnaire of demonstrated validity (Cohen, Dibble, Grawe, & Pollin, 1975; Nichols & Bilbro, 1966) was used, as results from such questionnaires have been shown to have good agreement with results from tests using blood or genetic markers (McGuffin, Owen, O’Donovan, Thapar, & Gottesman, 1994). The questionnaire (described by Levy et al., 2001) contains 12 questions such as “Does their mother ever confuse them in appearance?”, “Do they have very similar personalities?”, and “Do they have the same blood group?” to assess how similar the twins appear to be in terms of appearance, personality, and biology. All opposite-sex pairs were assigned as dizygotic.

Analyses

Exploratory analysis of the data was performed using SPSS software (SPSS Inc., 2003). Point prevalences were calculated to find the proportion of the sample affected by ADHD as defined by the published cut-offs for the DSM-IV and RD scales. Differences in groups defined by zygoty, age, and sex were then investigated, and regression and Mann–Whitney tests (McGuffin et al., 1994) were performed to explore the significance of any differences found. Only sex differences were found and so the data were standardised by sex.

The raw scores for the ATBRS were very negatively skewed with a “floor effect” whereby a high proportion of the sample had low scores. To achieve a closer approximation to normality, the data were transformed by taking the logarithm of each

score. This was also true for the scores for the other scales, so similar transformations were performed on those.

All model fitting was performed using the Mx package (Neale, 1997). First, univariate modelling was performed on each ADHD subtype and on the total scores of each of the other scales. The model fitting was performed using the logic as laid out in Neale and Cardon (1992), whereby first a model containing variance components for additive genetics (A), common environment (C) and non-shared environment (E) is examined (see Levy, Hay, & Bennett, 2006), and then nested submodels are trialled and compared for best fit. If two models have a similar fit to the data, the simpler one (involving fewer variables and degrees of freedom in the model-fitting) is accepted for parsimony. For example, first the ACE model is fitted and the χ^2 and p values noted. The AE model is then tested and if the χ^2 for the AE model does not appreciably reduce the fit, given the extra degree of freedom, then the AE is accepted to be the better fitting model. This is repeated with the CE model and the values again compared to see if it fitted better than the AE or ACE models. The results of the model fitting give the heritability with respect to the components being tested in the model; for example, a heritability of 60% comprises an additive genetic component of 60% and 40% common plus non-shared environment. The non-shared environment includes any error of measurement and is thus, in the absence of any real environmental effects, an estimate of reliability.

Next bivariate model fitting was performed on the ADHD data against the other scales, using the correlation of within and between twin scores on each scale. This was performed to explore any shared and exclusive inheritance between ADHD symptoms, as measured by the ATBRS, and the other disorders as measured by their scales. The same logic was followed for the fitting of bivariate models as for the univariate but with the added complexity of examining variance components between, in addition to within, each disorder.

Results

Prevalence

There are no published cut-offs for CD and ODD on the measures used so both of these disorders were treated as continua. The prevalence of RD using the published cut-off (Shaywitz, Shaywitz, Fletcher, & Escobar, 1990; Willcutt et al., 2000; Willcutt & Pennington, 2000) was 6% ($N = 215$) in our sample, which is comparable with the rate found in control groups in previous studies (APA, 2000 ; Friedman, Chhabildas, Budhiraja, Willcutt, & Pennington, 2003).

The prevalence of ADHD was split into its subtypes as presented in Table 1. Responding “Pretty much/Often” or “Very much/Often” to six or more items of inattentive and/or hyperactive-impulsive symptoms followed the DSM-IV classification (APA, 1994). The table indicates there is an approximately 2:1 ratio of males:females affected.

Table 1. Prevalence of ADHD symptoms by sex

| | Male (%) | Female (%) | Total (%) |
|-----------------------|-------------|---------------|--------------|
| Inattentive | 122 (7) | 58 (3) | 180 (5) |
| Hyperactive/impulsive | 20 (1) | 23 (1) | 43 (1) |
| Combined | 139 (8) | 61 (4) | 200 (6) |
| Total | 281 (16) | 142 (8) | 423 (12) |

Note: Data presented as total number (group percent).

Age, Sex, and Zygosity

Regression was performed by age for each scale in order to determine any age effects. The tests were performed separately for each sex and zygosity in addition to the whole sample. For all the tests, the r^2 values ranged from -0.001 to 0.000 and the analysis of variance p values from 0.343 to 0.769 , indicating no detectable age effects.

Mann–Whitney tests were performed for zygosity and sex effects. Again the tests were performed separately on the subgroups and the whole sample. For zygosity there were no effects with p values ranging from 0.147 to 0.969 . For sex, all scales showed a significant effect ($p < 0.001$), demonstrating that males had significantly higher mean scores on all of the ATBRS. All scores were then standardised by sex and the test performed again to check that the sex effects had been removed prior to modelling.

Univariate Modelling

The results of the univariate modelling on ADHD symptoms are presented in Tables 2 and 3. There are three degrees of freedom, so if the full ACE model is fitted there is a perfect fit. Reducing this to AE frees one degree of freedom to test the consequences of dropping C.

It can be seen that for inattentive (ADHD-I, $r_{mz} = 0.86$, $r_{dz} = 0.45$) and hyperactive-impulsive (ADHD-HI, $r_{mz} = 0.86$, $r_{dz} = 0.45$) subtypes, the ACE model is best, although common environment makes a relatively small contribution compared with additive genetics. The ACE model is also the best fit for the combined subtype (ADHD-C, $r_{mz} = 0.88$, $r_{dz} = 0.53$), but with a larger common environmental component. These results are as expected from the MZ/DZ correlations, where for ADHD-I and ADHD-HI the MZ correlation is roughly twice the DZ, which

Table 2. Univariate best-fitting models for the three ADHD subtypes

| ATBRS scale | A | C | E |
|---------------------------------------|------|------|------|
| ADHD-I ($p = 1.00$, $\chi^2 = 0$) | 0.81 | 0.04 | 0.14 |
| ADHD-HI ($p = 0.95$, $\chi^2 = 0$) | 0.83 | 0.03 | 0.14 |
| ADHD-C ($p = 1.00$, $\chi^2 = 0$) | 0.69 | 0.19 | 0.13 |

Table 3. Univariate best-fitting models for RD, CD, and ODD

| Scale | A | C | E |
|-----------------------------------|------|------|------|
| RD ($p = 1.00, \chi^2 = 0$) | 0.83 | 0.04 | 0.12 |
| CD ($p = 0.92, \chi^2 = 0.91$) | 0.88 | – | 0.12 |
| ODD ($p = 0.94, \chi^2 = 0.80$) | 0.85 | – | 0.15 |

suggests additive genetics, but much less than twice for ADHD-C, which suggests the presence of common environmental effects.

The results of the univariate modelling for RD, CD, and ODD are presented in Table 3. As with ADHD-C, the ACE model is the best fit for RD symptoms ($r_{mz} = 0.88, r_{dz} = 0.46$), although the common environmental effect is much smaller. As with the subtypes other than combined, there is a relatively small contribution from common environmental influences. For CD ($r_{mz} = 0.89, r_{dz} = 0.42$) and ODD ($r_{mz} = 0.85, r_{dz} = 0.45$), the AE model gives the best fit and both show a large genetic component (88% for CD and 85% for ODD).

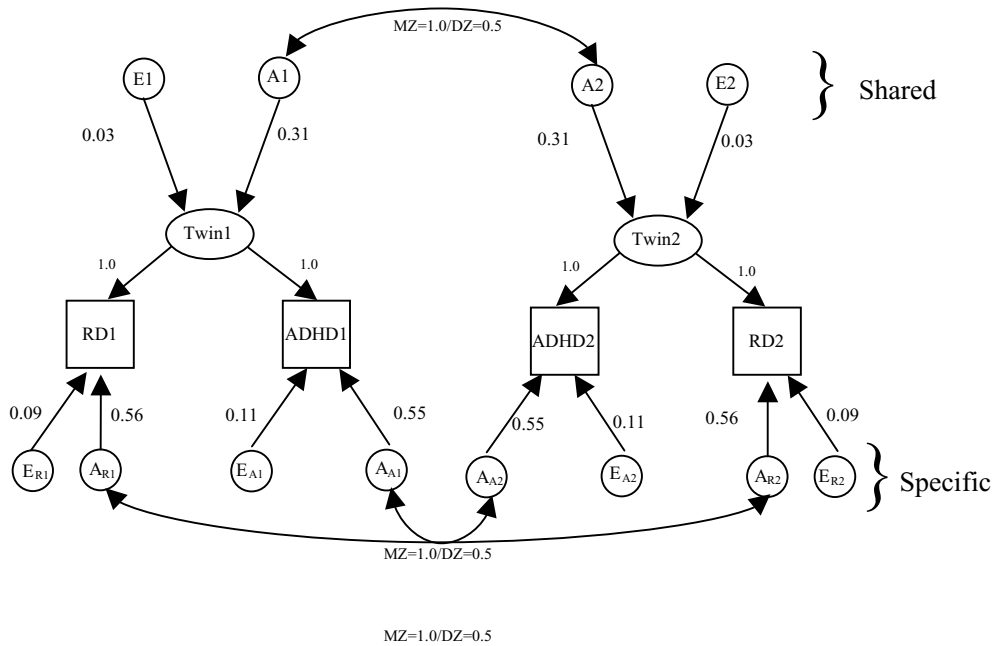
Bivariate Modelling

Each of the subtypes of ADHD was modelled separately against each of the other disorders (example model shown in Figure 1). Figure 1 shows the psychometric model used in these analyses. The shared components are shown at the top of the figure, while disorder-specific effects are at the bottom of the figure. For example, the genetic variance specific to RD may include aspects of cognition that have less overlap with inattention, while processes related to concentration would be contained in the shared variance.

The correlations between the measures are presented in Table 4.

Reading Disability. Table 5 presents the results for the modelling of ADHD and RD. The strongest association seen in this table is between the inattentive subtype and reading disability, with fairly poor fits for the models involving the hyperactive/impulsive or combined subtypes. Even though the univariate analyses for each had small common environments, the bivariate model shows no such effects. There is a shared genetic component of 31% between inattention and reading disability. Each then has its own sizeable, specific genetic component (55% for inattentive and 56% for reading disability).

Conduct Disorder. Table 6 presents the results for the modelling of ADHD and CD. The strongest association seen in this table is between the hyperactive/impulsive subtype and CD. There is a shared genetic component of 37% between disorders, but each has its own sizeable, specific genetic component (49% for hyperactive/impulsive and 52% for Conduct Disorder).



Note:

- A= Additive genetic effects common to ADHD and RD
- E= Non-shared environmental effects common to ADHD and RD
- AR/A = Additive genetic effects specific to RD/ADHD
- ER/A = Non-shared environmental effects specific to RD/ADHD
- RD = Reading Disability symptoms (1 =twin 1, 2 = twin2)
- ADHD = ADHD symptoms (1 =twin 1, 2 = twin2)
- MZ = monozygotic correlation
- DZ = dizygotic correlation

Figure 1. Psychometric bivariate path diagram of Predominantly Inattentive (ADHD-I) and Reading Disability (RD) disorders

Oppositional Defiant Disorder. Table 7 presents the results for the modelling of ADHD and ODD. The strongest association seen in this table is between the hyperactive/impulsive subtype and ODD. There is a shared genetic component of 42% between disorders, with a small shared common environmental component of 6%.

Table 4. Correlations between the measures

| | ADHD-I | ADHD-HI | ADHD-C | RD | CD | ODD |
|---------|--------|---------|--------|-------|-------|-------|
| ADHD-I | 1.000 | 0.435 | 0.856 | 0.348 | 0.346 | 0.445 |
| ADHD-HI | 0.435 | 1.000 | 0.782 | 0.223 | 0.383 | 0.526 |
| ADHD-C | 0.856 | 0.782 | 1.000 | 0.308 | 0.404 | 0.549 |
| RD | 0.348 | 0.223 | 0.308 | 1.000 | 0.174 | 0.180 |
| CD | 0.346 | 0.383 | 0.404 | 0.174 | 1.000 | 0.777 |
| ODD | 0.445 | 0.526 | 0.549 | 0.180 | 0.777 | 1.000 |

Table 5. Best fitting bivariate models for ADHD and RD

| | Shared | | | ADHD only | | | RD only | | |
|---|--------|------|------|-----------|------|------|---------|---|------|
| | A | C | E | A | C | E | A | C | E |
| ADHD-I ($p = 0.46$, $\chi^2 = 13.91$, $df = 14$) | 0.31 | – | 0.03 | 0.55 | – | 0.11 | 0.56 | – | 0.09 |
| ADHD-HI ($p = 0.06$, $\chi^2 = 23.34$, $df = 14$) | 0.18 | – | 0.02 | 0.67 | – | 0.12 | 0.69 | – | 0.10 |
| ADHD-C ($p = 0.04$, $\chi^2 = 22.05$, $df = 12$) | 0.21 | 0.06 | 0.03 | 0.49 | 0.11 | 0.09 | 0.61 | – | 0.08 |

Each then has its own specific genetic component (38% for hyperactive/impulsive and 36% for ODD). Interestingly, in this model the shared genetic component is larger than the disorder-specific components, thus implying that the comorbidity is due largely to a shared set of genetic influences rather than to a combination of specific components.

Table 6. Best fitting bivariate models for ADHD and CD

| | Shared | | | ADHD only | | | CD only | | |
|---|--------|------|------|-----------|------|------|---------|---|------|
| | A | C | E | A | C | E | A | C | E |
| ADHD-I ($p = 0.35$, $\chi^2 = 15.39$, $df = 14$) | 0.35 | – | 0.02 | 0.50 | – | 0.12 | 0.55 | – | 0.10 |
| ADHD-HI ($p = 0.58$, $\chi^2 = 12.34$, $df = 14$) | 0.37 | – | 0.01 | 0.49 | – | 0.12 | 0.52 | – | 0.10 |
| ADHD-C ($p = 0.07$, $\chi^2 = 19.87$, $df = 12$) | 0.34 | 0.06 | 0.02 | 0.38 | 0.08 | 0.10 | 0.50 | – | 0.10 |

Table 7. Best fitting bivariate models for ADHD and ODD

| | Shared | | | ADHD only | | | ODD only | | |
|--|--------|------|------|-----------|------|------|----------|---|------|
| | A | C | E | A | C | E | A | C | E |
| ADHD-I ($p = 0.22$, $\chi^2 = 17.65$, $df = 14$) | 0.45 | – | 0.01 | 0.41 | – | 0.13 | 0.40 | – | 0.14 |
| ADHD-HI ($p = 0.93$, $\chi^2 = 6.37$, $df = 13$) | 0.42 | 0.06 | 0.03 | 0.38 | – | 0.10 | 0.36 | – | 0.12 |
| ADHD-C ($p = 0.73$, $\chi^2 = 8.70$, $df = 12$) | 0.41 | 0.12 | 0.03 | 0.30 | 0.04 | 0.09 | 0.33 | – | 0.12 |

Discussion

The prevalences of ADHD and RD were found to be comparable with those found in previous studies. It was also found that ADHD symptoms occurred at a higher rate in males than females (at a ratio of approximately 2:1), which is also in line with previous studies. The univariate analyses demonstrated that all of the disorders have a strong genetic component. For the ADHD subtypes and RD there was also a modest shared environmental component.

The bivariate analyses showed that RD is most strongly linked with ADHD-I, with a shared genetic heritability of 31%. CD was most strongly linked with ADHD-HI, with a shared genetic heritability of 37%. There was a smaller but reasonable relationship to ADHD-I with a shared genetic heritability of 35%. ODD was most strongly linked with ADHD-HI with a shared genetic heritability of 42%, but there were lower correlations with both ADHD-C and ADHD-I.

The strong comorbidity between RD and ADHD-I (31% shared heritability), as opposed to between RD and the other ADHD subtypes (20% shared heritability), is what one would expect intuitively and is in agreement with previous studies (Friedman et al., 2003; Stevenson, 2001). Particularly, Stevenson, found exactly 30% of phonological awareness overlapped between RD and ADHD. Inattention and deficits with concentration, as characterised by ADHD-I, would make it very difficult for a child to learn to read, but this can also work in the other direction. The next step, to tease apart the nature of the shared heritabilities, begs the following questions: Do affected children display RD symptoms simply because ADHD-I symptoms make learning to read difficult or is some other, complex, shared pathway at work? Is there some shared factor, such as shared genes, which increases risk of both RD and ADHD-I, which is entirely separate from influences causative of either disorder alone? Does the presence of one disorder cause symptoms of the other, but not the other disorder (Willcutt et al., 2000)? It could also be that both disorders share a common subset of risk factors so elevated factors of one lead to an increase in the likelihood of the other. In future work, with a larger sample, this can be explored by comparing rates of comorbidity in extreme scoring inattentive twin and sibling pairs. In doing so a test of whether a high symptom count for one disorder is usually accompanied by an elevated count in the other can be made. Furthermore, the use of both twins and siblings will allow further exploration of the nature of the genetic factors involved.

The strong comorbidity of ODD and CD with ADHD-HI is also what one would expect from the observed symptoms of inappropriate behaviour and over-activity, and agrees with previous work (Dick, Viken, Kaprio, Pulkkinen, & Rose, 2005). As with the RD and ADHD-I comorbidity, more work is required to elucidate how it is mediated. Mannuzza, Klein, Abikoff, and Moulton (2004) found ADHD in children to be a predictor of CD in later life whether or not the child had CD. Other studies (Satterfield & Schell, 1997) disagree with this and highlight another limitation of research in this area. Both studies defined CD in different ways, both to each other and to the present study. Mannuzza et al. used clinically diagnosed CD,

Satterfield and Schell used criminality, while in this present study we used a short questionnaire measure. This means that a true comparison of the results is not entirely possible as each study is examining different phenotypes. Unfortunately with so many different ways of defining each disorder (questionnaires versus clinical interviews, self-report versus parent-report versus teacher-report) it becomes very difficult to make a valid comparison of results between studies, as at best they are examining overlapping phenotypes but not necessarily identical ones. This could also explain the disagreement between the current study and work by Volk et al. (2005) in which no differences were found in the rate of comorbidity of a variety of disorders with the ADHD subtypes.

It has been argued that the co-occurrence of these disorders may be an artefact of sampling using clinical populations (Caron & Rutter, 1991), since people may initially present because of either disorder, or may be more likely to present with both disorders. For example, children with ADHD-I are much less likely to present clinically than those with ADHD-C (Sawyer et al., 2004), and reading difficulties may be the reason why their inattention comes to the attention of the school or a clinician. As the present sample is non-clinical and is population based, such biases to an overestimate of comorbidity are unlikely, as supported by other work (Fergusson & Horwood, 1992).

A limitation of our study, however, is that all data are taken from questionnaire reports from a single rater. This means the results must be seen in light of both rater bias and shared method variance. Rater bias means that a particular person may give different subjective ratings of the same observed phenotype/behaviours, compared with another rater. It has been shown that mothers and teachers have biases that can produce differing conclusions from the same sample (Martin et al., 2002). Shared method variance is where two unrelated variables may be linked simply because they were collected using the same method (Willcutt et al., 2000). In this case, data were collected solely via questionnaire and so this cause of bias must also be investigated. Future work is planned to perform formal clinical interviews on a subset of the group. By comparing results from interviews and questionnaires we will be able to remove shared method variance and also add self-reports to the parent rated data in order to obtain a clearer picture than with a single source of data.

Implications for Practice

Hay and Levy (2001) discussed at length the implications of the genetics of ADHD for clinics and schools, but a few specific points should be noted. Not only do all these behaviours have a substantial genetic component, but there is a very modest role for common family environment, the opposite of what the proponents of “bad parenting” have postulated. The only exception is ADHD-C, where the combination of inattention and hyperactivity/impulsivity with the generally higher rates of comorbidity in this group (Levy et al., 2005) makes for a difficult family environment, which affects all family members. McDougall, Hay, and Bennett (in press)

identify the impact especially of ADHD-C on anxiety problems in siblings, and particularly the co-twin of a DZ twin with ADHD.

At the same time, the high genetic component has implications for parenting style. Parents may not reach criteria for ADHD (Hay, McStephen, & Levy, 2001), but may have problems with organisation and with impulse control that limit their ability to implement consistent parenting practices that assist their child(ren) with ADHD. Technically this is called genotype–environment correlation, where the child(ren) do not just have the genes for ADHD, but also an environment that fails to limit ADHD-related behaviour.

While this study has only touched on the extent of comorbidity in ADHD, it has raised a most interesting issue for clinicians and teachers. Namely, why does comorbidity happen and what can be done to limit its impact? Given the scepticism of some individuals about the existence of ADHD, some legitimacy comes from the finding that it often occurs in association with conditions such as RD where there is not the same uncertainty. It is clear that there are many different pathways to comorbidity and that combined behavioural and molecular genetic studies are contributing to an understanding of why, and thus how to address the issue.

Acknowledgments

This work was funded by a grant from the National Health and Medical Research Council of Australia. The authors would like to thank Grant Baynam and Kellie Bennett for their assistance with data collection and entry, and the cooperation of so many families, as well as the Australian Twin Registry.

References

- American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders* (4th ed.). Washington, DC: Author.
- Bates, T. C., Castles, A., Coltheart, M., Gillespie, N., Wright, M., & Martin, N. G. (2004). Behaviour genetic analyses of reading and spelling: A component processes approach. *Australian Journal of Psychology*, *56*, 115–126.
- Biederman, J., Faraone, S., Keenan, K., Knee, D., & Tsuang, M. (1990). Family-genetic and psychosocial risk factors in DSM-III Attention Deficit Disorder. *Journal of the American Academy of Child and Adolescent Psychiatry*, *29*, 526–533.
- Caron, C., & Rutter, M. (1991). Comorbidity in child psychopathology: Concepts, issues and research strategies. *Journal of Child Psychology and Psychiatry*, *32*, 1063–1080.
- Cohen, D. J., Dibble, E., Grawe, J. M., & Pollin, W. (1975). Reliably separating identical from fraternal twins. *Archives of General Psychiatry*, *32*, 1371–1375.
- Dick, D., Viken, R., Kaprio, J., Pulkkinen, L., & Rose, J. (2005). Understanding the covariation among childhood externalizing symptoms: Genetic and environmental influences on conduct disorder, attention deficit hyperactivity disorder, and oppositional defiant disorder symptoms. *Journal of Abnormal Child Psychology*, *33*, 219–229.
- Faraone, S. V., Biederman, J., & Friedman, D. (2000). Validity of DSM-IV subtypes of attention-deficit/hyperactivity disorder: A family study perspective. *Journal of the American Academy of Child and Adolescent Psychiatry*, *39*, 300–307.

- Fergusson, D., & Horwood, L. (1992). Attention deficit and reading achievement. *Journal of Child Psychology and Psychiatry*, 33, 375–385.
- Friedman, M., Chhabildas, N., Budhiraja, N., Willcutt, E., & Pennington, B. (2003). Etiology of the comorbidity between RD and ADHD: Exploration of the non-random mating hypothesis. *American Journal of Human Genetics*, 120B, 109–115.
- Gayán, J., & Olson, R. K. (2001). Genetic and environmental influences on orthographic and phonological skills in children with reading disabilities. *Developmental Neuropsychology*, 20, 483–507.
- Graetz, B. W., Sawyer, M. G., Hazell, P., Arney, F., & Baghurst, P. (2001). Validity of DSM-IV ADHD subtypes in a nationally representative sample of Australian children and adolescents. *Journal of the American Academy of Child and Adolescent Psychiatry*, 40(12), 1410–1417.
- Hay, D. A., & Levy, F. (2001). Implications of genetic studies of attentional problems for education and intervention. In F. Levy & D. A. Hay (Eds.), *Attention genes and ADHD* (pp. 214–224). East Sussex, UK: Brunner-Routledge.
- Hay, D. A., Bennett, K. S., McStephen, M., Rooney, R., & Levy, F. (2004). Attention deficit-hyperactivity disorder in twins: A developmental genetic analysis. *Australian Journal of Psychology*, 56(2), 99–107.
- Hay, D. A., McStephen, M., & Levy, F. (2001). The developmental genetics of ADHD. In F. Levy & D. A. Hay (Eds.), *Attention genes and ADHD* (pp. 58–79). East Sussex, UK: Brunner-Routledge.
- Levy, F., & Hay, D. (Eds.). (2001). *Attention, genes and ADHD*. East Sussex, UK: Brunner-Routledge.
- Levy, F., Hay, D., & Bennett, K. S. (2006). Genetics of ADHD: A current review and future prospects. *The International Journal of Disability, Development and Education*, 53, 5–20
- Levy, F., Hay, D. A., Bennett, K., & McStephen, M. (2005). Gender differences in ADHD subtype comorbidity. *Journal of the American Academy of Child and Adolescent Psychiatry*, 44, 368–376.
- Levy, F., Hay, D., McLaughlin, M., Wood, C., & Waldman, I. (1996). Twin sibling differences in parental reports of ADHD, speech, reading and behaviour problems. *Journal of Child Psychology and Psychiatry*, 37, 569–578.
- Levy, F., Hay, D., Waldman, I., & McStephen, M. (2001). Common family environment and comorbidity in ADHD. *ADHD Report*, 10, 9–14.
- Loo, S. K., Fisher, S. E., Francks, C., Ogdie, M., MacPhie, I., Yang, M., et al. (2004). Genome-wide scan of reading ability in affected sibling pairs with attention-deficit/hyperactivity disorder: Unique and shared genetic effects. *Molecular Psychiatry*, 9, 485–493.
- Mannuzza, S., Klein, R., Abikoff, H., & Moulton III, J. (2004). Significance of childhood conduct problems to later development of conduct disorder among children with ADHD: A prospective follow-up study. *Journal of Abnormal Child Psychology*, 32, 565–573.
- Martin, N., Scourfield, J., & McGuffin, P. (2002). Observer effects and the heritability of childhood Attention-Deficit Hyperactivity Disorder symptoms. *British Journal of Psychiatry*, 180, 260–265.
- McDougall, M., Hay, D. A., & Bennett, K. (in press). Having a cotwin with Attention Deficit Hyperactivity Disorder. *Twin Research and Human Genetics*.
- McGuffin, P., Owen, M., O'Donovan, M., Thapar, A., & Gottesman, I. (1994). *Seminars in Psychiatric Genetics*. London: Gaskell.
- Milberger, S., Faraone, S., Biederman, J., Testa, M., & Tsuang, M. (1996). New phenotype definition of attention deficit hyperactivity disorder in relatives for genetic analyses. *American Journal of Medical Genetics*, 67, 369–377.
- Neale, M. C. (1997). *Mx: Statistical modelling*. Richmond, VA: Department of Psychiatry, Virginia Institute for Psychiatric and Behavioral Genetics.
- Neale, M. C., & Cardon, L. R. (1992). *Methodology for genetic studies of twins and families*. Dordrecht, The Netherlands: Kluwer Academic Publishers.

- Neuman, R., Heath, A. C., Reich, W., Bucholz, K. K., Madden, P. A. F., Sun, L., et al. (2001). Latent class analysis of ADHD and comorbid symptoms in a population sample of adolescent female twins. *Journal of Child Psychology and Psychiatry*, *42*, 933–942.
- Nichols, R. C., & Bilbro, W. C., Jr. (1966). The diagnosis of twin zygosity. *Acta Genetica et Statistica Medica*, *16*, 265–275.
- Satterfield, J., & Schell, A. (1997). A prospective study of hyperactive boys with conduct problems and normal boys: Adolescent and adult criminality. *Journal of the American Academy of Child and Adolescent Psychiatry*, *36*, 1726–1735.
- Sawyer, M. G., Rey, J. M., Arney, F. M., Whitham, J. N., Clark, J. J., & Baghurst, P. A. (2004). Use of health and school-based services in Australia by young people with attention-deficit/hyperactivity disorder. *Journal of the American Academy of Child and Adolescent Psychiatry*, *43*, 1355–1363.
- Scourfield, J., Van den Bree, M., Martin, N., & McGuffin, P. (2004). Conduct problems in children and adolescents: A twin study. *Archives of General Psychiatry*, *61*, 489–496.
- Shaywitz, S., Shaywitz, B., Fletcher, J., & Escobar, M. (1990). Prevalences of reading disability in boys and girls. *Journal of the American Medical Association*, *264*, 998–1002.
- SPSS for Windows, Rel. 12.0.1 (2003). Chicago, IL: SPSS Inc.
- Stevenson, J. (2001). Comorbidity of reading/spelling disability and ADHD. In F. Levy & D. A. Hay (Eds.), *Attention, genes, and ADHD* (pp. 99–114). East Sussex, UK: Brunner-Routledge.
- Taylor, E., Dopfner, M., Sergeant, J., Asherson, P., Banaschewski, T., Buitelaar, J., et al. (2004). European clinical guidelines for Hyperkinetic Disorder—First upgrade. *European Child and Adolescent Psychiatry*, *13*(Suppl. 1), 7–30.
- Thapar, A., Harrington, R., & McGuffin, P. (2001). Examining the comorbidity of ADHD-related behaviours and conduct problems using a twin study design. *British Journal of Psychiatry*, *179*, 224–229.
- Volk, H., Neuman, R., & Todd, R. (2005). A systematic evaluation of ADHD and comorbid psychopathology in a population-based twin sample. *Journal of the American Academy of Child and Adolescent Psychiatry*, *44*, 768–775.
- Waldman, I. D., Rhee, S. H., Levy, F., & Hay, D. A. (2001). Causes of the overlap among symptoms of ADHD, Oppositional Defiant Disorder, and Conduct Disorder. In F. Levy & D. A. Hay (Eds.), *Attention, genes, and ADHD* (pp. 115–138). East Sussex, UK: Brunner-Routledge.
- Willcutt, E., & Pennington, B. (2000). Comorbidity of reading disability and attention-deficit/hyperactivity disorder: Differences by gender and subtype. *Journal of Learning Disabilities*, *33*, 179–191.
- Willcutt, E., Boada, R., Pennington, B., & Riddle, M. (in press). A parent-report screening questionnaire for learning difficulties in children.
- Willcutt, E., Pennington, B., & DeFries, J. (2000). Twin study of the etiology of comorbidity between reading disability and attention-deficit/hyperactivity disorder. *American Journal of Medical Genetics*, *96*, 293–301.
- Willcutt, E. G., Pennington, B. F., Smith, S. D., Cardon, L. R., Gayan, J., Knopik, V., et al. (2002). Quantitative trait locus for reading disability on chromosome 6p is pleiotropic for ADHD. *American Journal of Medical Genetics (Neuropsychiatric Genetics)*, *114*, 260–268.