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**A Longitudinal Analysis of the Effects of Genetic and  
Family Factors on Attention Deficit Hyperactivity Disorder**

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## Abbreviations

<b>-2LL</b>	Minus two times the log likelihood
<b>A</b>	Additive genetic
<b>AGFI</b>	Adjusted goodness of fit index
<b>AIC</b>	Akaike's Information Criterion
<b>ADHD</b>	Attention Deficit Hyperactivity Disorder
<b>CaStANET</b>	Cardiff Study of All Wales and North West of England Twins
<b>CBCL</b>	Child Behavior Checklist
<b>CRPBI</b>	Children's Report of Parental Behavior Inventory
<b>CD</b>	Conduct Disorder
<b>CI</b>	Confidence Interval
<b>C</b>	Shared environmental
<b>DSM</b>	Diagnostic and Statistical Manual of Mental Disorders
<b>DZ</b>	Dizygotic
<b>D</b>	Non-additive genetic
<b>E</b>	Non-shared environmental
<b>FES</b>	Family Environment Scale
<b>FR</b>	Father report
<b>GxE</b>	Gene-environment interaction
<b>GFI</b>	Goodness of fit index
<b>IYFP</b>	Iowa Youth and Family Project
<b>ICD-10</b>	International Classification of Disease 10 <sup>th</sup> revision
<b>MR</b>	Mother report
<b>MZ</b>	Monozygotic
<b>MTA</b>	Multimodal Treatment Study of Children with ADHD



<b>NICHD</b>	National Institute of Child Health and Human Development
<b>OS</b>	Opposite sex
<b>ODD</b>	Oppositional Defiant Disorder
<b>PR</b>	Parent report
<b>rGE</b>	Gene-environment correlation
<b>SWFS</b>	South Wales Family Study
<b>SDQ</b>	Strengths and Difficulties Questionnaire
<b>SWAN</b>	Strengths and Weaknesses of ADHD symptoms and Normal behaviour scale

## Summary

Previous studies suggest that both genetic and environmental factors contribute to variation in Attention Deficit Hyperactivity Disorder (ADHD) symptoms and their continuation. Family relationship factors have also been associated with the disorder. However, whether these family relationship factors have a causal effect on ADHD symptoms is not clear. This thesis used two longitudinal community samples, to examine the effects of both genetic and family relationship factors on ADHD symptoms.

The first sample included 1214 families (twins and a parent) from a population based twin register (twins aged 12-20 years). A longitudinal sub-sample of 833 families from data collected 8 years previously was also used. The second sample included 309 children (aged 11-14 years) and their parents who took part in a longitudinal study on two occasions 12 months apart.

ADHD symptoms and their continuation from childhood to adolescence and young adulthood were found to be influenced by genetic factors ( $h^2 = 64\%$ ; genetic factors explained 78% of stability), however non-shared environmental factors were also significant. Father-child rejection was the only relationship factor to significantly impact on ADHD symptoms ( $\gamma = .11$ ;  $\beta = .15$ ). ADHD symptoms were shown to have a negative impact upon mother-son hostility, mother-child rejection and family conflict ( $\gamma = .13$  to  $.22$ ;  $\beta = .19$  to  $.24$ ). ADHD symptoms and parent-child warmth were not associated. The association of both mother- and father-child hostility with ADHD symptoms was genetically mediated ( $r_a = .41$  to  $.58$ ). Importantly, the association between mother-son hostility and boys' ADHD symptoms was environmentally mediated as well ( $r_e = .20$ ).

The findings suggest the importance of establishing whether or not environmental factors, such as family relationship factors, have causal effects on ADHD symptoms. The majority of the results in this thesis suggest that ADHD symptoms have a negative impact upon family relationship factors.

## **Papers arising from work within this thesis**

Lifford, K. J., Harold, G. T. & Thapar, A. (2008). Parent-child relationships and ADHD symptoms: A longitudinal community sample. *Journal of Abnormal Child Psychology*, 36, 285-296.

Lifford, K. J., Harold, G. T. & Thapar, A. (in press). Parent-child hostility and child ADHD symptoms: A genetically sensitive and longitudinal analysis. *Journal of Child Psychology and Psychiatry*.

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## **Thesis Overview**

This thesis, divided into six chapters, examines the effects of genetic and family relationship factors on Attention Deficit Hyperactivity Disorder (ADHD) symptoms. The first chapter reviews previous research and discusses concepts related to the thesis. This chapter is therefore an introduction to the whole thesis and closes with the presentation of the aims of the thesis. Following this, Chapter 2 describes the two study samples, a population based twin study and a longitudinal community sample, which are used to address the aims of the thesis in subsequent chapters. This second chapter also outlines the statistical analyses which are used in the subsequent chapters. Chapter 3 utilises one of the study samples (the twin sample) to examine genetic and environmental influences on ADHD symptoms and their continuation. The fourth chapter examines whether warmth and hostility in the parent-child relationship may have a causal risk effect on ADHD symptoms. This utilises both study samples to firstly examine the extent to which any association is genetically and environmentally mediated and to secondly examine the direction of influences in these associations. Chapter 5 explores the longitudinal associations between ADHD symptoms and both parent-child rejection and family conflict. Comparisons are drawn between the association of mother-child rejection and ADHD symptoms and the association of father-child rejection and ADHD symptoms. The association between family conflict and ADHD symptoms is examined in both the genetically informative and the longitudinal community sample. The results pertaining to chapters 3, 4 and 5 are discussed within these respective chapters. The final chapter discusses the results of the preceding chapters as a whole as well as discussing the strengths and limitations of the thesis. Finally, practice implications which have arisen from the contents of the thesis are discussed.

## **Chapter 1. Introduction**

This thesis examines the effects of both genetic and family relationship factors on child and adolescent symptoms of Attention Deficit Hyperactivity Disorder (ADHD). Two community samples are utilised. The influence of genetic factors on ADHD and its continuation will be examined using a population based twin sample. Specific family relationships, such as dimensions of the parent-child relationship (warmth, hostility and rejection), will be investigated with regard to the nature of their association with ADHD. That is, whether these family relationship factors have a causal effect on ADHD symptoms will be examined. This will be done using two methods. Firstly, the extent to which the association between these family relationship factors and ADHD is genetically or environmental mediated will be addressed using the twin sample. Secondly, the extent to which these specific family relationship factors have an impact upon ADHD symptoms and vice versa will be examined using a longitudinal community based sample.

This chapter will firstly discuss ADHD, its clinical presentation, epidemiology and aetiology. This will be followed by a discussion of the importance of establishing environmental factors as having risk effects, the challenges to this and how they may be overcome. Next, I will discuss the role of parent-child relationships and their impact upon children's behaviour, giving a brief summary of the psychological theories relevant to this. Following this I will discuss research which specifically investigates the association between family relationship factors and ADHD. Next I will discuss gene-environment interaction for ADHD. Lastly I will conclude and present the aims for this thesis.

## **Attention Deficit Hyperactivity Disorder**

### *Clinical Features of Attention Deficit Hyperactivity Disorder and its Epidemiology*

Attention Deficit Hyperactivity Disorder (ADHD) is a childhood neurodevelopmental disorder which is characterised by inattention, overactivity and impulsivity. A form of the disorder was first reported in the 1900s by George Still (Barkley, 1998). Throughout the 19<sup>th</sup> Century the nature of the disorder was reviewed and refined with various causes having been suggested along with the different configuration of symptoms (Barkley, 1998). Under the current diagnostic guidelines for the UK (International Classification of Disease 10<sup>th</sup> revision; ICD-10, World Health Organisation, 1993) and the USA (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; DSM-IV, American Psychiatric Association, 2000), ADHD (or hyperkinetic disorder as it is referred to in ICD-10) consists of the key characteristics detailed above. Both diagnostic criteria include 9 inattention symptoms, of which 6 must have persisted for at least 6 months (American Psychiatric Association, 2000; World Health Organisation, 1993). However ICD-10 requires at least 3 hyperactivity symptoms (out of 5) and at least 1 impulsivity symptom (out of 4), whereas DSM-IV indicates at least 6 hyperactivity/impulsivity symptoms (out of 9) should be met, but also allows for the diagnosis of ADHD subtypes. Both diagnostic criteria require an onset of symptoms before / no later than age 7 years and there is also a requirement of pervasiveness of symptoms across situations (e.g. school and home).

Measurement of ADHD for the purposes of diagnosis includes assessment of the child, interview of the parents and information from the teacher. Diagnostic criteria are then used from either DSM or ICD. For research purposes however ADHD can also be measured at a trait level using questionnaires. These instruments

include those such as the DuPaul rating scale (1991), the Conner's rating scale (1973) the Strengths and Difficulties Questionnaire (SDQ; Goodman, 1997), the Strengths and Weaknesses of ADHD symptoms and Normal behaviour scale (SWAN; Swanson, Schuck et al., 2008) and the Attention Problems subscale of the Child Behavior Checklist (CBCL; Achenbach, 1991). The correlations among these questionnaires and with ADHD measures as well as their use for screening for ADHD both give weight to being able to assess ADHD symptoms using them (Pelham, Fabiano & Massetti, 2005).

Levy and colleagues (Levy, Hay, McStephen, Wood & Waldman, 1997) showed that ADHD appears to act on a continuum. They found that heritability estimates were similar whether a categorical measure was used or a continuous one, thus suggesting in a highly heritable disorder the amount of variation over the continuum that can be explained by genes is the same as that can be explained in a category of ADHD vs. non-ADHD (Levy et al., 1997). Similarly Gjone, Stevenson and Sundet (1996) found that heritability estimates remained similar with increasing severity of ADHD symptoms. While ADHD is taken as a distinct disorder, it therefore seems to be the case that children affected by the disorder could be regarded as high scorers on a continuum. Using ADHD as a categorical measure is important primarily for diagnosis and treatment, and therefore also for studies examining the effects of medication and other treatments. However, it is also useful to be able to use a trait measure of ADHD symptoms within a community sample so that referral bias is not included (Woodward, Dowdney & Taylor, 1997). If ADHD does indeed act along a continuum as research suggests, it is important to understand how processes might work within the population not just for those high scorers who are diagnosed (or just sub-clinical).

In the UK, the prevalence of childhood ADHD ranges from approximately 1% to 2.2% depending on whether criteria of ICD-10 hyperkinetic disorder or DSM-IV ADHD is used (Ford, Goodman & Meltzer, 2003; Meltzer, Gatwood, Goodman & Ford, 2003). In the USA prevalence rates appear higher, probably due to the differences in diagnostic criteria, with Faraone and Doyle (2001) reporting that between 2 and 10% of the population are affected. Worldwide, a recent report suggests ADHD affects just over 5% of children and adolescents (Polanzyk, de Lima, Horta, Biederman & Rohde, 2007).

As with other neurodevelopmental disorders there is a gender bias in ADHD, with more males being affected than females. The ratio of males to females is between 6:1 and 9:1 in clinical samples and 3:1 in community samples (Gaub & Carlson, 1997). These differences could to some extent be the result of referral bias, as suggested by Biederman and Faraone (2005). They suggest that inattentive symptoms are more covert than hyperactivity and impulsivity symptoms and as girls are more affected by the inattentive subtype there could be a referral bias due to the symptom presentation (Biederman & Faraone, 2005). Similarly, clinically referred females with ADHD show less comorbid symptoms than males (Biederman, Mick et al., 2002; Gaub & Carlson 1997), such as oppositional defiance and conduct problems and this could explain the referral bias (as those with comorbid problems may be more likely referred). However, in non-referred samples, comorbidities have been found to be similar for males and females with ADHD (Biederman, Kwon, et al., 2005). These gender differences found to a greater extent in clinical samples than in non-referred samples, highlight one of the advantages of using community studies, as these show less of a gender difference and are not affected by referral bias.

Children with ADHD tend to be from lower socio-economic classes (Biederman & Faraone 2005) and score lower on tests of IQ (Tripp, Ryan & Peace, 2002). Within a sample of children with ADHD, low socio-economic status and verbal IQ have been shown to have an effect on the severity of hyperactive and impulsive symptoms (Langley, Holmans, van den Bree & Thapar, 2007). Scahill et al. (1999) also found an association between low income and ADHD in a community sample of children.

### *Comorbidity*

There is a high rate of comorbidity between ADHD and a number of other psychological problems (Taylor et al., 2004). Many children with ADHD also suffer with oppositional defiant disorder (ODD), conduct disorder (CD), anxiety and depression (Spencer, Biederman & Mick, 2007). Ford et al. (2003) examined the mental health of children in the UK in 1999 and showed that of the children with ADHD (DSM-IV diagnosis used) 26.6% also had ODD, 17.7% had CD and a further 8.2% had not otherwise specified disruptive disorder. Childhood ADHD (hyperactivity) has been shown to influence later conduct problems (Taylor, Chadwick, Heptinstall & Danckaerts, 1996). Not only this, but children with ADHD and comorbid conduct problems tend to have worse outcomes (Thapar, van den Bree, Fowler, Langley & Whittinger, 2007).

Comorbidity is particularly characteristic of referred populations. In a comparison of boys who had been referred for hyperactivity (UK sample) with those who had not been referred, conduct problems were a predictor of referral as well as being highly associated with parental coping (Woodward, Downey & Taylor, 1997). However the strongest predictor of referral was emotional disturbance (but sub-

clinical levels as those with emotional disorders were excluded), thus suggesting that comorbidities were a strong predictor of referral for ADHD (Woodward et al., 1997). The authors therefore concluded that clinical samples of children with ADHD are not necessarily representative of the general population of children with ADHD (Woodward et al., 1997).

### *Life course of ADHD*

With age, the symptoms of ADHD tend to decrease (Faraone, Biederman & Mick, 2006) through adolescence into adulthood, however for some people a diagnosis still remains in adulthood. Faraone, Biederman & Mick (2006) conducted a review of follow up studies and reported that the persistence rate for ADHD symptoms one year later was 83%, which increased to 96% when 2 studies which appeared to be outliers were removed. Using this meta-analysis they predicted that at age 25 years the rate of persistence of ADHD diagnosis would be 15%, whereas a partial remission (termed residual diagnosis) was estimated to have a rate of between 40 and 60% at age 25 years (Faraone et al., 2006). A more recent study of children with ADHD and control comparisons followed them up after one, four and ten years at which point they were in late adolescence and young adulthood (Biederman et al., 2006). All cases were diagnosed with DSM-III-R ADHD at referral and after 10 years showed a persistence rate of 70% (and 8% in the controls). More recently in a non-referred population, Hurtig and colleagues (2007) selected those who fulfilled diagnostic criteria in childhood (retrospectively) and adolescence. They found that 39% of those with childhood ADHD had remitted in adolescence but the other 61% continued to have symptoms even if their subtype of ADHD diagnosis had changed somewhat (Hurtig et al., 2007). It therefore appears that while there is evidence of a

decrease in ADHD from childhood into adolescence there is still a reasonable amount of continuation of ADHD into adolescence.

Even though there does appear some decline in ADHD during adolescence, adulthood ADHD is becoming increasingly recognised (Adler, Newcorn & Faraone, 2007). However there are still problems with diagnosis and treatment for adult ADHD. For example, the only medication which is licensed for adult ADHD is the non-stimulant drug atomoxetine, and this is only recommended if it has been prescribed as a child (Nutt et al., 2007). In terms of diagnosis, the issue remains that the criteria for childhood ADHD are not developmentally appropriate for adults (Nutt et al., 2007). Also, adults have to have had symptoms in childhood as well as persistent and current symptoms in adulthood to obtain a diagnosis (Spencer, Biederman & Mick, 2007).

In community samples, the stability of ADHD symptoms has been shown to be moderate, with correlations of between  $r = .4$  and  $r = .6$  over 2 to 6 years in adolescence and young adulthood (aged between 11 and 22 years; Achenbach, Howell, McConaughy, & Stranger, 1995; Ferdinand, Verhulst & Witznitzer, 1995). Those with high scores tend to remain high scorers and those with lower scores tending to stay lower as the ranking is relatively stable (Achenbach et al., 1995; Ferdinand et al., 1995). Twin studies on population based samples have also shown moderate correlations of ADHD symptoms across time. For example, between the ages of 8 and 14 years, Larsson, Larsson and Lichtenstein (2004) found a stability correlation of  $r = 0.51$  and similarly Rietveld, Hudziak, Bartels, van Beijsterveldt, and Boomsma, (2004) found slightly higher stability correlations of between  $r = 0.65$  and  $0.75$  in twins aged between 7 and 12 years. A recent population based study of twins which used both diagnostic criteria as well as population based ADHD categories



(from latent class analyses), showed relatively low rates of ADHD persistence over 5 years (Todd et al., 2008). Only 28% remained as having any ADHD diagnosis after 5 years, with even lower percentages for those remaining in the same subtype group. Using their population based latent classes, the greatest stability was found for severe combined type ADHD which showed 35% of those continuing to have this after 5 years (Todd et al., 2008).

### *Negative outcomes of ADHD*

A number of impairments are faced by children with ADHD, including problems at school, poor academic achievement and disruptions in family and social relationships. For example, Manuzza and colleagues (Manuzza, Klein, Bessler, Malloy & LaPadula, 1993) followed up boys into young adulthood who had been diagnosed with hyperkinetic disorder as children and found that they had on average 2.5 years less education than the control group. They also showed that while cases and controls were matched on parental socio-economic status, the types of work participants were employed in were lower in occupational ranking for those who had a diagnosis of hyperactivity in childhood compared with the controls (Manuzza et al., 1993). There were more in the hyperactive group who did manual jobs and owned small businesses, whereas the control group included more who did professional jobs. In a UK sample followed up in late adolescence, Taylor and colleagues (1996) showed that poor achievements in school, social problems and poor relationships with peers were all significant outcomes for children with ADHD. Biederman et al. (2006) found evidence for a higher lifetime prevalence of psychiatric disorder and in a previous study reported substance use problems particularly for girls with ADHD (Biederman, Mick et al., 2002).

Epidemiological studies are not quite so conclusive in their evidence for particular negative outcomes of ADHD. Hofstra, van der Ende and Verhulst (2002) showed that once other problems had been taken into account, attention problems did not significantly predict any adult DSM-IV diagnoses. But as the authors do point out, caution should be taken with these results because at follow up self reports were used and ADHD symptoms are more often reported by others rather than the person themselves (Hofstra et al., 2002). Fergusson, Horwood and Ridder (2007) also found that once conduct problems had been controlled for the effect of attention problems on later substance use and abuse was reduced (compared with before controlling for conduct problems) and in many cases non-significant. They suggest that this offers supporting evidence to their previous proposal that conduct problems are associated with later substance use, psychiatric outcomes and criminal behaviour whereas attention problems are more associated with poor academic outcomes (Fergusson et al., 2007).

### *Aetiology of ADHD*

#### *Genetics*

Family studies have shown that ADHD is familial for both males and females (Biederman, Faraone, Keenan, Knee & Tsuang, 1990; Biederman, et al., 1992; Faraone et al., 2000). There is a 2 to 8 fold increase in risk for having ADHD in first degree relatives of those with ADHD compared to those without (Faraone & Doyle, 2001). However, as these family studies cannot disentangle genetic and family environment factors, genetically sensitive designs have been used to examine the extent to which the familial nature of ADHD is due to genetic and environmental factors.

Adoption studies from the 1970s suggested a genetic basis of ADHD (Cantwell, 1975). More recently Sprich, Biederman, Crawford, Mundy & Faraone (2000), compared the rate of ADHD in relatives of both adopted and non-adopted children who had been diagnosed with ADHD. Consistent with a genetic basis of ADHD, Sprich et al. (2000) found higher rates of ADHD in the relatives (biological) of children with ADHD who had not been adopted compared with the relatives (adoptive) of those who had been adopted. Not only this, but they also showed that the rates of ADHD in the relatives of adopted children with ADHD were comparable to a control group of children referred to paediatric clinics but not with ADHD (Sprich et al., 2000).

A number of twin studies have shown a large amount of the variation of ADHD to be due to genetic variability, with heritability estimates in the region of 60 to 88% (Rutter 2006). Studies have examined ADHD using different rating scales, both symptom counts and categorical cut offs and in a wide range of age groups and countries and have shown a large amount of the variance in ADHD symptoms can be accounted for by genetic factors (e.g. Gjone et al., 1996; Goodman & Stevenson, 1989; Haberstick et al., 2008; Hudziak, Derks, Althoff, Rettew, & Boomsma, 2005; Martin, Scourfield & McGuffin, 2002; Nadder, Silberg, Eaves, Maes, & Meyer, 1998; Polderman et al., 2007; Rietveld, et al., 2004; Thapar, Harrington, Ross & McGuffin, 2000). Both additive and non-additive genetic influences have been shown to contribute along with non-shared environmental influences (Hudziak et al., 2005; Rietveld et al., 2004). In other studies only additive genetic and non-shared environmental influences on ADHD symptoms have been found (e.g. McLoughlin, Ronald, Kuntsi, Asherson & Plomin, 2007). Shared environmental influences, that is environmental factors which make twins more similar, tend to be small or non-

significant. Rater contrast effects, that is where one twin is scored as higher on ADHD symptoms and the other in contrast scores much lower, have also been shown for mothers' reports of their children's ADHD symptoms in a number of twin studies (e.g. Thapar, Hervas & McGuffin, 1995; Simonoff et al., 1998). These have been examined in more detail and understood as reporter bias rather than sibling interaction (Simonoff et al., 1998). However, even in studies which have found rater contrast effects, genetic factors still play a considerable role.

Gender differences in the magnitude of genetic and environmental influences on ADHD symptoms have been examined using twin studies. Many of these have not shown significant gender differences (e.g., Thapar et al., 1995; Simonoff et al., 1998, Hudziak et al., 2005), but some have (e.g. Rhee, Waldman, Hay & Levy, 1999; Steffensson et al., 1999; Larsson et al., 2004). Gender differences in the proportion of variation in ADHD symptoms which can be accounted for by genetic and environmental factors will therefore be discussed further and tested within the third chapter of this thesis.

Molecular genetic studies have also shown ADHD to be influenced by genetic factors (Thapar, Langley, Owen & O'Donovan, 2007). However, as a likely polygenic disorder (many genes having an influence) studies have shown a number of gene variants to be associated with the disorder. Results from these studies are not always replicated, thus evidence is stronger for some of the gene variants such as in the dopamine receptor genes *DRD4* and *DRD5* than in other genes such as the dopamine transporter gene *DAT1 (SLC6A3)* and the serotonin transporter gene *SLC6A4* (Thapar et al., 2007). Variation in findings have been suggested to possibly come about because of gene-environment interaction (GxE; e.g. Langley, Turic et al., 2008), that is only within certain environments do the genotypes confer risk, alternatively only

those with a particular genotype may be more susceptible to particular environmental pathogens (Rutter, 2006). This concept of GxE will be discussed later.

A recent meta-analysis of studies investigating the effects of the dopamine system genes, showed significant pooled odds ratio for the *DRD4* 7-repeat allele, the *DRD4* 5-repeat allele and the *DRD5* 148-bp allele but no evidence of an association between ADHD and *DAT1* 480-bp allele (Li, Sham, Owen & He, 2006). There was however also evidence of protective effects of the *DRD4* 4-repeat allele as well as the *DRD5* 136-bp allele (Li et al., 2006). Therefore evidence for the involvement of the dopamine system genes is quite strong. These genes are candidate genes because of the way that stimulant medication acts on the brain (e.g. Solanto, 2002).

#### *Genetic influences on the continuation of ADHD*

Twin studies have shown that genetic factors are important not only in the aetiology of ADHD but they also account for a large proportion of the stability of ADHD (Kuntsi, Rijdsdijk, Ronald, Asherson & Plomin, 2005; Larsson et al., 2004; Larsson, Lichtenstein & Larsson, 2006; Price et al., 2005; Rietveld et al., 2004; van den Berg, Willemsen, de Geus & Boomsma, 2006). However even though there are genetic influences on the stability and change in ADHD symptoms over time, environmental factors are also shown to play a role. This has been shown in studies using a range of different age groups from preschoolers, middle childhood to young adulthood (e.g. Price et al. 2005, Larsson et al., 2004). These longitudinal twin studies of the continuation of ADHD symptoms have also shown mixed results for whether there are gender differences. Those including young children or older adolescents, while showing some mean or variance gender variation, do not suggest that there are gender differences in the magnitude of genetic and environmental influences on

ADHD symptoms (Kuntsi et al., 2005; Price et al., 2005; van den Berg et al., 2006). In middle childhood and adolescence however studies suggest that there may be some gender differences (Larsson et al., 2004; Larsson et al., 2006; Rietveld et al., 2004). The genetic and environmental influences on ADHD symptoms and their continuation will be examined in the third chapter of this thesis. An examination of whether there are gender differences in the genetic architecture of ADHD symptoms and their continuation will also be included in Chapter 3 of this thesis along with further discussion of the studies mentioned here. The twin sample included in this thesis covers a different age span to the previously reported twin studies and therefore examination of this sample will be an important addition to the current evidence.

There are very few molecular genetic studies which have focused on the continuation of ADHD symptoms. There is evidence however which suggests that the DRD4 7-repeat allele is associated not only with the aetiology of ADHD but also its continuation (El-Faddagh, Laucht, Maras, Vöhringer & Schmidt 2004; Langley Fowler et al., 2008).

### *Environmental Factors*

While there is much evidence that there are strong genetic influences on ADHD, the environment also plays a role. Twin studies have shown heritability to be high, but not equal to one. Similarly, a number of studies have examined the effects of different environmental factors. Of these factors, the particular focus of this thesis is to examine family relationships. Other environmental factors which show evidence of association with ADHD will also be discussed here (low birth weight and maternal smoking during pregnancy). While these environmental factors have been associated with ADHD, establishing whether they are causal is difficult (Academy of Medical

Sciences, 2007). Following the brief discussion of findings for the associated environmental factors a discussion of establishing causal risk factors will be provided.

#### *Family relationship factors*

Studies of families with children with ADHD have shown higher levels of conflict within the family when compared with control families (Biederman et al., 1995a; Biederman et al., 1995b; Biederman, Faraone & Monuteaux, 2002). Not only this, Biederman (1995a) found that an increasing number of family adversities, as measured by Rutter's adversity indicators (which had previously been associated with increases in childhood psychopathology), was associated with ADHD. However other studies do not show such associations (Brown & Pacini, 1989) or find that the associations are no longer evident once other factors such as conduct problems or depression are taken into consideration (George, Herman & Orstrander, 2006). This thesis focuses particularly on examining the association between dimensions of the parent-child relationship and ADHD symptoms. Family relationship factors, especially aspects of the parent-child relationship, and their association with ADHD will therefore be discussed in more detail later.

#### *Low birth weight*

Both low birth weight and preterm birth have been associated with ADHD. In a meta-analysis of studies examining the outcomes of preterm births, Bhutta, Cleves, Casey, Craddock and Anand (2002) found significantly greater attention problems in those who were preterm (and low birth weight) compared to controls, as well as increased rates of diagnosis of ADHD. Using MZ twin pairs where one had ADHD

and the other did not, the effect of low birth weight on ADHD outcome has also been shown to be an environmental mediated risk (Lehn et al., 2007).

### *Smoking during pregnancy*

A number of studies have shown that maternal lifestyle factors such as smoking and drinking alcohol during pregnancy are associated with ADHD in children (Linnett et al., 2003; Langley, Rice, van den Bree & Thapar, 2005). For example using a case control design, Mick and colleagues (Mick, Biederman, Faraone, Sayer & Kleinman, 2002) report the risk for ADHD to be doubled by maternal smoking during pregnancy. Also there was a significant association between alcohol use during pregnancy and ADHD (Mick et al., 2002). The association between smoking during pregnancy and ADHD is more robust than that between alcohol use and ADHD, for which the association has been described as inconsistent (Linnett et al., 2003). In a review of published articles, Langley and colleagues (2005) found a pooled odds ratio of more than 2 for the increase in risk for ADHD of children whose mothers smoked during pregnancy. Also, within a sample of children with ADHD smoking during pregnancy has also been shown (along with low socio-economic status) to have an effect on the severity of hyperactive and impulsive symptoms (Langley et al., 2007). However, more recent evidence suggests that maternal smoking does not have a causal effect on ADHD symptoms as there is evidence that this association is genetically mediated (Thapar, et al., submitted).

### **Establishing Causal Effects of Environmental Risk Factors**

The evidence presented in the previous section highlighted the association between ADHD and three environmental factors: family relationship factors, low



birth weight and smoking during pregnancy. Even though these are associated however, establishing whether these environmental factors have causal effects on ADHD is important not only for understanding the effects of these environmental factors, but also for possible interventions or treatments of ADHD, as well as for studies which examine the effects of GxE.

While there may be an association between an environmental factor and an outcome such as child psychopathology, there may be a number of explanations to the associations other than a causal effect (Rutter, 2007). These include both reverse causation and genetic confounds (Rutter, 2007). That is, firstly an environmental factor may indeed be a consequence of the supposed outcome measure rather than being a risk factor. Secondly, an association between an environmental factor and an outcome may come about because of genetic factors which influence both (Rutter, 2007).

The possibility of there being a genetic confound comes about because of correlations between genetic and environmental risk factors, that is, gene-environment correlation. This will now be discussed in more detail.

### *Gene-Environment Correlation*

Gene-environment correlation (rGE) has been described as genetic influence on exposure to risk environments (Rutter & Silberg 2002). People who are at high genetic risk also tend to experience risk environments and therefore the two risk factors are associated (Rutter, 2006). There are three possible mechanisms by which this comes about, active, evocative and passive rGE. Active rGE comes about because people seek out certain (risk) environments because of aspects of their behaviour or personality that are genetically influenced. Evocative rGE, is very similar to active

rGE (and therefore hard to distinguish from it) but differs in that people elicit responses from others because of their genetically influenced behaviour. Passive rGE comes about as the risk environments may be created by parents (which is associated with genetically influenced behaviour of the parent), parents' genes are also associated with children's genes and thus the two are correlated.

A number of studies have examined the influence of genetic factors on family relationships and have shown these to be significant (e.g. Herndon, McGue, Krueger & Iacono, 2005; Kendler & Baker, 2007, Lichtenstein et al., 2003; McGue, Elkins, Walden & Iacono, 2005; Neiderhiser, Reiss, Lichtenstein, Spotts & Ganiban, 2007). For example, significant genetic influences have been found for female adult twins' recall of warmth in both maternal and paternal relationships, with heritability estimates of 32% and 27% respectively, and shared environmental influences also being important (explaining 35% and 47% of the variance respectively; Lichtenstein et al., 2003).

While these studies have shown evidence of rGE, they do not show evidence of the process through which rGE may be at work. Active and evocative rGE are similar in that they both work through the child either eliciting responses or seeking out experiences and therefore are characterised by children having an impact on their environments because of their genetically influenced behaviours and actions. This therefore makes distinguishing between these two types of rGE a matter of examining what the children are either eliciting in others or seeking. In contrast, passive rGE comes about because children share genes with their parents and their parents' genes which are shared with their child also impact the parental behaviour which creates the child's environment.

Neiderhiser et al. (2004) noted a way to distinguish between active/evocative rGE and passive rGE by comparing results from twin children studies and twin mum studies. The logic is that evocative/active rGE is implied if child-based twin designs show genetic influences, while parent-based twin designs will show environmental influences on parent-child relationship. In contrast for passive rGE, child-based designs will show shared environmental effects whereas parent-based designs will show genetic influences (Neiderhiser et al., 2004).

*rGE: From correlations to mechanisms*

Adoption studies provide a study design that is able to assess not only the presence of rGE but also how this may come about, through children's behaviour problems. Specifically examining evocative rGE for affective and disciplinary aspects of parenting, Ge, Conger et al. (1996) found an association between a child's family history of psychiatric disorder and their adoptive parents' parenting, thus supporting evidence of rGE. There was also evidence that children's anti-social/hostile behaviour was associated with their biological parents' psychiatric disorder status and that children's behaviour was associated with their adoptive parents' disciplinary parenting. Moreover, the associations between children's behaviour and both their biological parents' psychiatric disorder status and their adoptive parents' disciplinary parenting accounted for the association between biological parent disorder and adoptive parenting thus showing mediation and therefore the mechanism through which the rGE comes about (Ge, Conger et al., 1996). Interestingly, they also showed effects of adoptive mothers' parenting on child behaviour but not fathers' so suggesting bidirectional influences between child behaviour and mothers' parenting. O'Connor, Deater-Deckard, Fulker, Rutter, & Plomin (1998) used a longitudinal

study to examine similar relationships and showed that the rGE was mediated through the child's externalising behaviour problems. However, they conclude that the evidence was only modest because while externalising behaviours were found to mediate the relationship between biological parents' psychiatric disorder status and adoptive parents' parenting, the reduction in the original association was small (O'Connor et al., 1998). There was also some evidence of an environmentally mediated effect of parenting on children's externalising behaviour once genetic association had been controlled for (O'Connor et al., 1998).

As the results from these adoption studies have shown, even though evidence suggests that children's genes influence their family environment (i.e. genetic influences on environmental factors), this in itself does not tell us about how this environmental factor is associated with a behavioural outcome (Rutter, Pickles, Murray & Eaves, 2001). Just because an environment and a behavioural outcome are both genetically influenced and both associated with one another does not mean that the relationship between them is genetically influenced (i.e. that the same genetic influences act on the environment and on the behaviour; Rutter, et al., 2001). It is therefore important to take care to not mix up the notion of genetic influences on an environmental variable with environmental or genetic mediation of a risk effect on an outcome variable (Rutter, 2006). The former is an examination of the origins of a variable and the latter is an examination of the mechanism through which a variable (whether genetically or environmentally influenced itself) has its effect.

#### *Testing for Environmentally Mediated Risk Effects*

To test whether an environmental factor has a true causal effect on an outcome it is necessary to take any genetic association between the two variables into

consideration because the genetically mediated association confounds the true effect of the environmental factor on the outcome variable. There is evidence for this genetically mediated association being important. For example, life events and depression are associated partly because of shared genetic effects (Thapar, Harold & McGuffin, 1998). Studies have shown true environmentally mediated effects of risk variables on outcomes such as anti-social behaviour. For example, using a genetically informative sample Jaffee, Caspi, Moffitt and Taylor (2004) showed that maltreatment had an environmentally mediated effect on children's anti-social behaviour once association due to genetic factors had been taken into account.

For studies to be able to assess whether an environmental factor has a true risk effect on the outcome of interest Rutter (2005) suggests a number of criteria should be met. Studies should be capable of pulling apart genetic and environmental effects, such as twin or adoption studies, they should also be longitudinal so that the direction of a causal effect can be examined. Thirdly, the accurate measurement of the environmental factor is important as well as fourthly, obtaining a sample large enough to test for significant effects. The final two criteria for a study to test for a true environmental risk effect are that the design enables the pitting of two hypotheses against each other (e.g. environmental vs. genetic mediation) and secondly that the assumptions of the study design are stated and tested (Rutter, 2005).

### **The Parent-Child Relationship and Children's Behaviour**

Having discussed the aetiology and epidemiology of ADHD as well as the importance of testing whether an environmental factor has a true causal risk effect, in this section I discuss the evidence for the association between the parent-child relationship and children's behaviour. This includes a discussion of the parent-child

relationship in family and environmental contexts and an overview of the relevant psychological theories pertaining to the role of the parent-child relationship in children's development in general (the following section focuses more specifically on aspects of the parent-child relationship and the association with children's ADHD symptoms). Finally this section includes a discussion of bidirectional associations. These bidirectional associations are important to examine due to the possibility of reverse causation being an explanation for the association between an environmental risk factor, such as dimensions of the parent-child relationship, and an outcome such as children's behaviour.

Historically the psychological literature has understood parenting and the parent-child relationship to be a substantial influence on children. Therefore, much of the research into the association between parent-child relationships and children's behaviour has hypothesised the relationship to be in this direction, even when cross sectional studies are being employed. While experimental study designs can examine the causal effects, cross sectional studies cannot. The use of longitudinal studies is therefore crucial in the absence of experiments, in being able to infer the direction of the effects of parent-child relationship on children and vice versa rather than using cross sectional studies which cannot reveal anything more than the association between the two.

### *The Parent-Child Relationship in Family and Environmental Contexts*

The dynamic nature of the parent-child relationship with influences both from child and parent is incorporated into a systems approach to the understanding of the family as a unit and as individuals within it (Minuchin, 1985). Within the family, relationships are not independent of each other, rather subsystems such as the parent-

child dyad or parent-parent dyad each have an impact upon and are impacted by other subsystems (Minuchin, 1985). Theories of child development which are based on systems theory are therefore dynamic as they recognise that changes within one subsystem have an impact upon other subsystems. This includes not just the nuclear family but also the wider social and cultural environment of the child. The development of the child is therefore influenced by the parent-child relationship as well as other relationships and environmental contexts. Therefore, while the parent-child relationship is important (as suggested by many other theories in psychology) other relationships also impact, albeit perhaps indirectly, upon children.

The literature on marital conflict also highlights the importance of the parent-child relationship as this is one of the mechanisms through which inter-parental conflict exerts its effect on children (Harold, Fincham Osborne & Conger, 1997; Davies, Harold, Goeke-Morey & Cummings, 2002; Harold & Howarth, 2004; Kaczynski, Lindahl, Malik, & Laurenceau, 2006). Explanations of this indirect process include family stress (the family is a system so relationships all influence each other), scapegoating (focusing on the child's behaviour problem rather than the inter-parental problem), modelling (children coping the way their parents interact) and socialization (inconsistent parenting having an effect on the child) (Erel & Burman, 1995). What is highlighted in each of these explanations is how the inter-parental conflict spills over into the parent-child relationship which then has a negative impact on the child.

Socio-economic status has also been shown to have indirect effects on children via the parent-child relationship, thus highlighting not only the importance of the parent-child relationship but also the context which this relationship is in. The Family Stress Model (Conger et al., 1992) was developed to explain the mechanism

through which economic hardship influences children and adolescents' adjustment and suggests that parenting is the main entity which impacts upon adolescents' development. Economic hardship however impacts upon perceptions of economic pressure which then has an influence on parental mood and marital conflict. Therefore this model is compatible with the spill over hypothesis of marital conflict and more broadly a systems approach, with economic hardship being an environmental context which affects subsystems within the family. Although some studies have shown direct pathways there is still a great deal of evidence highlighting the role of the parent-child relationship and parenting as the main pathway through which other factors (in this example economic hardship, marital conflict and parental mood) have an impact upon the child. Indeed, Costello and colleagues (2003) used a natural experiment to show that for those in poverty, a reduction in poverty had a positive effect on children's behaviour problem and this was mediated through a change in parenting (Costello, Compton, Keeler & Angold, 2003).

#### *Attachment, Parenting and Dimensions of the Parent-child Relationship*

The effect that parents have on their children is highlighted in the socialisation process and theories of child development. In attachment theory, Bowlby (1969) suggested the formation of a secure attachment between an infant and their mother (or primary caregiver) enables children to have a secure base from which to explore their environments and other relationships. While primarily a theory based on infants and their mothers, more recently suggestions have been made as to extensions of this theory which also examine attachment in early adulthood (Waters & Cummings, 2000; Waters, Hamilton & Weinfield, 2000). Using attachment theory as a basis, Ainsworth developed the "strange situation", an experimental paradigm, to assess



infants and categorise them as securely attached, insecure-avoidant, insecure-resistant or insecure disorganised-disoriented (Waters, Hamilton & Weinfield, 2000).

Interestingly however, some of her studies in other cultures suggest that dimensional aspects of the parent-child relationship such as warmth are not synonymous with a secure attachment (MacDonald, 1992).

Baumrind (1966) also used categories, but she used these to form parenting typologies aiming to capture different parenting styles and the impacts these had upon child rearing and children's behaviour. These different parenting types particularly focused on parental control, with the authoritative parenting being suggested as the most conducive to optimum outcome for children (Baumrind, 1966). This type of parenting was understood as giving children a degree of direction and discipline, in a manner which was child-centred and used explanation for restrictions. It also however, allowed the child a certain amount of autonomy and self-assertiveness. Authoritative parenting style therefore enabled children to learn from the outcomes of decisions made and punishments received for unacceptable behaviour (Baumrind, 1966).

More recently attempts have been made to integrate the notion of parenting style categories with more specific measures of parenting practices (Darling & Steinberg, 1993). Darling and Steinberg (1993) propose a model which suggests that parenting style serves as a general climate or context within which parenting practices have an effect on children's outcomes. Parenting practices are defined as being domain specific and therefore indicate specific responses or actions with regards to children's behaviour. As parenting style in contrast is more general, they propose that this has more of a moderating role in the effects of parenting practices on child outcome (Darling & Steinberg, 1993). This theoretical model therefore highlights the

importance of the context within which socialization takes place. Also, other aspects of the way parents relate to their children with regards to particular situations have been examined in a more dimensional manner. Dimensional aspects of the parent-child relationship such as the acceptance-rejection dimension (Rohner, Khaleque & Cournoyer, 2005) have therefore been used to understand the association between parent-child relationships and child outcomes rather than focusing on categories of parenting style.

Examining the emotional quality of the parent-child relationship has a long history particularly in the field of adult psychiatry. Originally the role of expressed emotion in relationships (which included warmth, hostility, criticism, emotional over-involvement, positive remarks) was of particular interest to researchers as an association had been shown between low expressed emotion and better recovery/lack of re-lapse for patients with schizophrenia (Brown and colleagues; for review see Hooley, 1985). Since then expressed emotion has been assessed in a number of disorders including child psychiatric conditions (Frye & Garber 2005; Hibbs et al., 1991; McCarty & Weisz, 2002; Schwartz et al., 1990; Vostanis, Nicholls & Harrington, 1994; Vostanis & Nicholls, 1995; Wearden, Tarrier, Barrowclough, Zastowny & Rahill, 2000).

Schwartz and colleagues (1990) examined the association between child psychopathology (depression, CD or substance abuse) and both maternal expressed emotion and parental psychopathology and found that maternal criticism was associated with an increased risk of having at least one of the disorders. Hibbs and colleagues (1991) found high expressed emotion to be more common in families of children with disruptive behaviour disorders or obsessive compulsive disorder than in families of normal control children. Vostanis, Nicholls and Harrington (1994), also

found an association between maternal expressed emotion and children's psychopathology. They found different associations however depending on the type of disorder and expressed emotion construct being examined (Vostanis, Nicholls & Harrington, 1994). In a follow up study however, Vostanis and Nicholls (1995) found that levels of expressed emotion did not predict change in children's symptoms.

More recently, McCarty and Weisz (2002) found criticism in the mother-child relationship to be associated with externalising behaviours in a sample of children referred to mental health outpatient clinics. Frye and Garber (2005) also found that children's externalizing behaviours were associated with mothers' criticism. However this was a longitudinal study and showed that children's externalising behaviour in 6<sup>th</sup> grade (age 11 years) significantly predicted mothers' criticism two years later. Indeed, externalising behaviour was shown to play a mediating role in the association between maternal depression history (chronicity and severity) and maternal criticism (Frye & Garber, 2005).

### *Effects of Parents on Children and Children on Parents*

The theories mentioned in the previous section highlight the importance of the parents and the effects that they have on children. However, children also play an active role in their socialization and may elicit particular parenting practices through their behaviour, thus reverse causation is a possibility.

Similar to the theories previously mentioned, social learning theory also suggests the importance of parents, but through imitation and modelling processes. Parental behaviours provides an example to children which they observe and experience and these are then modelled and imitated by children who therefore learn particular patterns of behaviour and responses. Based on this theory, Patterson

(Patterson, DeBaryshe & Ramsey, 1989; Reid, Patterson & Snyder, 2002) suggests that parental behaviour has an impact upon children specifically in terms of their aggressive behaviour. However, not only is the parental behaviour important, but the child's is also. The child's behaviour elicits parental responses and cycles of coercive behaviours from both parent and child are formed which result in the escalation of children's behaviour problems.

The notion that children have an effect on the way their parents behave towards them was introduced by Bell (1968). He challenged the assumption that the association between parental and child behaviour is driven so completely by the parents and suggested that children are also actively involved in the way they are parented because their behaviours elicit responses from their parents. The effects of children on their parents have since become more widely recognised and study designs which take these effects into account have been important in showing the effects that parenting has on children (Collins, Maccoby, Steinberg, Hetherington & Bornstein, 2000). However, some studies while acknowledging the possible effects of children on their parents are not always able to test for these effects due to the study designs employed.

One of the aims of this thesis is to use studies designs which allow for testing child effects on parents and parent effects on children in order to assess whether the aspects of the parent-child relationship have a causal risk effect on ADHD. A number of specific dimensional aspects of the parent-child relationship will be examined, including warmth, hostility and rejection, as well as examining both the mother-child and father-child relationship.

## **The Parent-Child Relationship and ADHD**

Given that ADHD is understood as a neurodevelopmental problem rather than a behavioural problem, the association between parent-child relationships and childhood *symptoms* may differ to that between parent-child relationships and *behaviour problems*. Much of the literature in child developmental psychology has focused on externalising problems. There is less research which has examined the association between family relationships and ADHD symptoms in community samples particularly in a longitudinal study. However, there is a great deal of theory and research that can inform studies of ADHD symptoms.

A number of studies have used externalising problems as an outcome measure to examine the impacts of parent-child and other family relationships. For example Forehand and Nousiainen (1993) found a significant effect of father acceptance on conduct problems but not mother acceptance. However this study was cross sectional and therefore the direction of this association was hypothesised rather than tested. Ge, Best, Conger and Simons (1996) used a longitudinal sample and found a significant effect of both mother and father hostility on conduct problems but only father warmth having an impact on child conduct problems. Different findings for the impact of the mother- and father-child relationship were also shown in a study conducted by the National Institute of Child Health and Human Development (NICHD) Early Child Care Research Network (2004). This longitudinal study of children initially aged 4½ years followed up to age 7-8 years showed that fathers' sensitivity predicted lower externalising problems. However, it was mothers' child-centred beliefs regarding education and child rearing which influenced externalising problems (NICHD Early Child Care Research Network, 2004).

Focusing specifically on ADHD symptoms, Carlson, Jacobvitz and Sroufe (1995) found that overstimulating and intrusive care-giving had a significant impact upon children's distractibility in preschool years and hyperactivity in mid-childhood (6-8 years). While these also had an impact upon hyperactivity at age 11 years, previous levels of hyperactivity were the best predictor of hyperactivity (Carlson et al., 1995). Gadeyne, Ghesquière & Onghena (2004) also looked at the longitudinal association between ADHD symptoms and aspects of parenting. They found mothers' restrictive control influencing attention problems as well as attention problems having an effect on mothers' restrictive control. For fathers however, their parenting did not impact upon ADHD symptoms, but children's ADHD symptoms had a significant effect on fathers' supportive parenting (Gadeyne et al., 2004). Jacobvitz, Hazen, Curran and Hitchens (2004) also showed that hostility within the family at age 2 years had a significant effect on ADHD symptoms at age 7 years. Thus there appears some evidence of parent-child and family relationships having an effect specifically on children's ADHD symptoms in community samples.

Institutional care has also been shown to be associated with inattention and overactivity (Kreppner, O'Connor, Rutter & the English and Romanian Adoptees Study Team, 2001). Children who spent longer in severely deprived institutional conditions (in Romanian orphanages) during their early childhood went on to display higher levels of overactivity and inattention in later childhood (aged 4, 6 and 11 years old) after being adopted into families in the UK than those who spent less time in the institutions (Kreppner et al., 2001; Stevens et al., 2008). Also, institutional care has been shown to be associated with lack of selective relationships, which was also associated with inattention and overactivity particularly for boys (Roy, Rutter & Pickles, 2004). While there appears to be an association of institutional care and

early relationships with ADHD, it is unclear whether inattentive and overactive behaviours in children who were in institutional care are indexing the same ADHD phenotype as usually found in clinical populations (Stevens et al., 2008).

Asarnow et al. (2001) made comparisons between children with depression, those with ADHD and controls (when trying to establish whether high expressed emotion was specific to children with depression or more generally to psychopathology). While they showed differences in expressed emotion between the depression group and both ADHD and control group, there was no difference between the ADHD and control group (Asarnow et al., 2001). In contrast however, Peris and Baker (2000) found expressed emotion measured in preschoolers to predict both externalizing behaviour and ADHD four years later. In a sample of girls (both with and without ADHD) Peris and Hinshaw (2003) also showed an association between high expressed emotion in mothers and ADHD. Mothers' expressed emotion was also associated with ODD/CD but to a lesser extent and once ODD/CD was controlled for expressed emotion was still associated with ADHD diagnosis (Peris & Hinshaw, 2003). Also the association was stronger between ADHD diagnosis and criticism than with emotional over-involvement.

Some of the association between dimensions of the parent-child relationship and ADHD could be due to ODD symptoms (Barkley, Fischer, Edelbrock & Smallish, 1991; Lange et al., 2005; Seipp & Johnston, 2005). For example, Lindhal (1998) found boys with no behaviour problems and those with ADHD to score similarly on family variables (marital dissatisfaction, overt hostility and conflict over child rearing) compared with those with ADHD and ODD or only ODD. However, a more recent study by Goldstein, Harvey and Freidman-Weieneth (2007) did not find differences between parenting measures of mothers of hyperactive children compared

with those mothers of children with both ODD and hyperactivity. When examining the trajectories of children, Jester and colleagues (2005) found that lower emotional support and intellectual stimulation from the parents were more likely to predict membership in the high inattentive/hyperactivity group when their aggression trajectory was held constant. Thus, when taking aggression into account, there was an association of these factors with inattentive/hyperactivity. In contrast, family cohesiveness was significant in predicting membership of the aggression trajectory when their inattentive/hyperactive trajectory was held constant (Jester et al., 2005).

Psychogiou and colleagues (2007, 2008) examined the role of parenting on ADHD symptoms in a non-clinical sample. Their studies specifically investigated how parental (both mothers' and fathers') ADHD symptoms may affect the association between parenting and ADHD symptoms. Their results suggest different relationships between parenting and child ADHD symptoms dependent on parental ADHD symptoms. They found support for a similarity-fit hypothesis for mothers, in that the effect of children's ADHD symptoms on parenting is ameliorated by mothers having a high ADHD score (Psychogiou, Daley, Thompson & Sonuga-Barke, 2007). In contrast, for fathers there appears a similarity mis-fit, where fathers with high ADHD symptoms' parenting is affected to a greater degree by children's ADHD symptoms than fathers' parenting where the father has low levels of ADHD symptoms (Psychogiou, Daley, Thompson & Sonuga-Barke, 2008). However these studies (Psychogiou et al., 2007; Psychogiou et al., 2008) were not longitudinal, thus establishing the direction of associations was not possible.

Experimental studies can also be used to suggest direction of effects between variables. By manipulating one variable such as a treatment or intervention condition, the effects on an outcome can be measured. Treatment studies for ADHD have



therefore been useful to examine the effects of successful treatment on parent-child interactions. Indeed, studies have shown that when stimulant medication effectively treats ADHD symptoms some improvements are seen in interactions between mothers and their sons (Barkley & Cunningham, 1979; Schachar, Taylor, Wieselberg, Thorley, & Rutter, 1987). However the study by Schachar and colleagues (1987) included children with ADHD and ODD or CD and therefore the associations could partly be due to reduction in these other behavioural problems. The largest ADHD treatment trial to date is the Multimodal Treatment Study of Children with ADHD (MTA). The assigned treatment aspect of the trial lasted for 14 months, however families were also followed up after 24 and 36 months in order to examine longer term effects (Swanson, Arnold et al., 2008).

The MTA has shown that medication which reduced ADHD symptoms (both medication and medication with behaviour therapy) also significantly improved negative discipline parenting compared with the community care comparison (Wells et al., 2000). They also showed that behavioural therapy alone improved negative parenting compared with the community comparison (Wells et al., 2000) even though the effect of behaviour therapy did not make as great an improvement on ADHD symptoms as the medication groups did during the time of the trial (MTA Cooperative Group, 1999). A more general parent-child relationship measure however showed that combined treatment (medication and behaviour therapy) and behaviour therapy both showed greater improvements in a composite measure of the parent-child relationship (power assertion and personal closeness) than the community care comparison group (MTA Cooperative Group, 1999). When examining positive parenting, this was shown not to differ across the four treatment groups (Wells et al., 2000). In contrast, when using observational measures of parent-child relationship, combined treatment

was shown to improve constructive parenting when compared with medication or community care groups (Wells et al., 2006). These results suggest interventions can improve the parent-child relationship, some of which occur alongside improvements in ADHD symptoms and some of which do not. Thus whether the parent-child relationship has a causal effect on ADHD symptoms is not clear cut because the associations could be due to improvements in the child's symptoms.

Therefore, while there is some evidence for negative family relationships being associated with ADHD symptoms, whether the relationships have a negative impact on the child's ADHD symptoms or vice versa or both, merits further investigations. One of the aims of this thesis is to examine this relationship in a longitudinal context to try to establish firstly if there is an association between family relationships and ADHD symptoms and secondly to ascertain the direction of influence.

#### *Continuation of ADHD and the role of family relationships*

As previously discussed, twin studies have shown that the continuation of ADHD symptoms are explained to a great extent by genetic factors. However, because the variation in ADHD symptoms is not completely explained by genetic influences it is important to try to ascertain and understand whether environmental factors such as dimensions of family relationships have a causal effect on ADHD symptoms. Longitudinal and twin studies can be used together to assess this.

Because there is some evidence that family relationships and ADHD symptoms are associated, family relationships may play a role in the continuation of symptoms. Regardless of whether parent-child relationships have an impact upon the initial development of ADHD symptoms they may be important for the continuation.

The notion of bidirectional associations between parents' and children's behaviours and coercive family processes suggest that patterns of interactions within the family could be instrumental in the maintenance of ADHD symptoms. Bernier and Siegel (1994) suggest a model in which children's behaviour impacts upon parental stress levels, which negatively affect their parenting and result in worsening ADHD symptoms. Also, as research has shown other factors such as socio-economic status and inter-parental conflict to indirectly affect children through the parent-child relationship, this supports the examination of the effect of parent-child relationships on symptoms as a more proximal factor.

Both Chapters 4 and 5 of this thesis examine the possible bidirectional association between parent-child relationships and ADHD in a longitudinal sample.

### **Gene-Environment Interplay**

There are a number of different ways in which interplay between genes and the environment may occur. These include, genetic influences on an environmental risk factor (rGE), genetic susceptibility to an environmental risk factor (GxE), environmental influences on gene expression, and differences in heritability according to variation in environments (Rutter, Moffitt & Caspi, 2006). I have already discussed rGE and its relevance to establishing an environmental risk factor. Here I will discuss GxE as this is a possible way through which genes and family relationship factors, particularly aspects of the parent-child relationship, may act together have an effect on ADHD and its continuation.

### *Gene-Environment Interaction*

An important reason for examining whether or not an environmental factor does indeed have an environmentally mediated effect is that once established as an environmental risk factor it is then a good candidate for possible GxE (Moffitt, Caspi & Rutter, 2005). If however the association is genetically mediated, any GxE found may in fact be gene-gene interaction (Sheese, Voelker, Rothbart, & Posner, 2007; Laucht et al., 2007). Because of the evidence presented thus far regarding the association between ADHD symptoms and family relationships that suggests possible bidirectional effects, it is therefore important to carefully examine the direction of influence as well as the genetic vs. environmental mediation of this association before continuing to examine GxE (Thapar, Harold, Rice, Langley & O'Donovan, 2007).

GxE is where the effect of an environmental risk factor is dependent on the genetic susceptibility, or vice versa that the level of risk environment may vary the genetic effect. Examples of GxE have been found for a number of health problems such as heart disease as well as children's mental health problems such as anti-social behaviour and depression (Feinberg, Button, Neiderhiser, Reiss & Hetherington, 2007; Rice, Harold, Shelton & Thapar, 2006; Rutter, 2006). Some studies of gene-environment interplay focusing on family relationships have found interactive effects on depression (Rice et al., 2006) and anti-social behaviour (Feinberg et al., 2007). However, as yet there are few studies focusing on ADHD which show evidence for gene-environment interplay (Thapar, Langley, Asherson & Gill, 2007).

Molecular studies of GxE and ADHD have examined family adversity as well as smoking and drinking alcohol during pregnancy. A number of different gene variants have been examined as the genetic component of the interaction. Therefore both the genetic and environmental factors are those which have been shown to be

associated with ADHD. Plausible theories regarding the way in which the GxE may be working can then be suggested. Also inconsistent findings in genetic studies (see earlier section on molecular genetic studies of ADHD) have been suggested to be perhaps due to GxE (e.g. Langley, Turic et al., 2008). Therefore examining those genotypes which show some evidence of association may yield significant associations under particular environmental conditions.

While not looking specifically at ADHD symptoms, Sheese et al. (2007) found an interactive effect of quality of parenting and *DRD4* (7-repeat allele) on young children's sensation seeking temperament but no GxE for effortful control. The study however was cross sectional and as the authors mention, the parenting measure was not very specific therefore did not offer much potential in understanding how this has an impact upon temperament. Focusing specifically on ADHD, Laucht et al. (2007) found significant interaction between two variable number of tandem repeat (VNTR) polymorphisms in the *DAT1* gene and family adversity as measured by a composite psychosocial adversity scale on ADHD symptoms. At the age of 15 years, psychosocial adversity factor, which was measured 3 months after birth, showed a main effect on ADHD. Five different *DAT1* variants were examined in their association with ADHD, none of which showed main effects. Two of the variants however showed significant GxE effects with *DAT1* having a significant effect on ADHD in high adversity participants (Laucht et al., 2007). More recently, a significant GxE effect of childhood environmental adversity and a polymorphism in the serotonin transporter promoter gene (5-HTTLPR) on childhood ADHD has been shown (Retz et al., 2008). Main effects were found for both childhood adversity and 5-HTTLPR genotype, and those exposed to high adversity and with the short-short or short-long genotypes were at particularly increased risk for ADHD. However, this

study used retrospective reports of childhood ADHD as well as quite a selected sample (of delinquents). Waldman (2007) examined a different family factor, maternal marital status, and found an interactive effect with a D2 dopamine receptor (*DRD2*) polymorphism (*TaqI*). Those with the risk genotype were at increased risk for ADHD only if their mothers were single (divorced, separated or never married). This study also showed evidence of a GxE interaction between the number of mothers' marriages and *DRD2* risk genotype, interestingly however this only became significant once other variables had been controlled for (Waldman, 2007).

Some (but not all) of these studies show main effects of the family environment measure, however as it has not been established whether these factors do indeed have a causal effect on ADHD these GxE studies while interesting are perhaps premature. The GxE results all need replicating in other studies as the few studies which have examined GxE of family environmental effects on ADHD are all different, in terms of the particular genotypes or the outcome measurement of ADHD. Indeed, before examining GxE it is important to establish that the environmental factor actually has a causal risk effect on ADHD. There is therefore a need to examine this.

Other GxE interactions which have been examined for their effects on ADHD include the environmental factors of smoking and alcohol during pregnancy. For example, Kahn, Khoury, Nichols and Lanphear (2003) investigated GxE effects of *DAT1* and smoking during pregnancy on ADHD. While no main genotype effect was found, maternal smoking during pregnancy showed increased risk for hyperactive/impulsive and oppositional scores in five year olds. The interaction between *DAT1* genotype and smoking during pregnancy was found to have an effect on hyperactive/impulsive scores as well as oppositional scores but not on inattentive

scores. Other studies since then have examined GxE effects on ADHD of maternal smoking during pregnancy and *DAT1*, as well as looking at a polymorphism within *DRD4* (Becker, El-Faddagh, Schmidt, Esser & Laucht, 2008; Brookes et al., 2006; Neuman, et al., 2007). There is some evidence of replication from the Becker et al. (2008) study, but the Neuman et al. (2007) found significant GxE for a different *DAT1* allele. Brookes et al. (2006) did not find evidence of GxE for maternal smoking and *DAT1* gene variants effects on ADHD, but they did find an interactive effect for maternal alcohol use during pregnancy. Furthermore, Langley, Turic and colleagues (2008) investigated GxE of alcohol and smoking during pregnancy and birth weight with four gene variants (within *DRD4*, *DAT1*, *DRD5* and *5-HTT*) on ADHD and found no significant interactions. However, when examining antisocial behaviours (CD and ODD) within ADHD, they showed some evidence for interactive effects between birth weight and both *DAT1* and *DRD5* as well as between maternal smoking in pregnancy and *DRD5* (Langley, Turic et al., 2008). However, again it is not clear whether these environmental factors are indeed causal and therefore the results should be considered with some caution.

## **Conclusions**

Previous evidence suggests that ADHD is highly heritable, however environmental factors have also been shown to contribute. It is not yet clear which environmental factors these are. A number of family relationship factors have been associated with ADHD but whether these have a causal role is not clear. This is important to establish both for interventions as well as for further research into GxE.

## **Aims**

Given the evidence presented in this chapter I will be addressing a number of aims in this thesis. Primarily the effects of genetic factors and family relationship factors on ADHD symptoms will be examined in the process of establishing whether these factors have a causal effect on ADHD symptoms. More specifically the following aims are addressed:

1. Establish the proportion of genetic and environmental variance on ADHD symptoms and its continuation.
2. Ascertain whether the contribution of environmental and genetic factors is similar for males and females.
3. Assess whether there is an association between family relationship factors and ADHD symptoms.
4. Where an association does exist (aim 3) ascertain whether this is genetically or environmentally mediated.
5. Establish whether there is a longitudinal relationship between family relationship factors and ADHD symptoms and in which direction the influence occurs.
6. Examine the role of both parent and child gender differences in the association between ADHD symptoms and dimensions of the parent-child relationship.



The following chapter outlines the study samples and methods used in this thesis. Chapter 3 addresses the first two aims and uses the twin study sample. Chapters 4 and 5 use both community studies to address aims 3, 5 and 6, with Chapter 4 also addressing aim 4.

## **Chapter 2. General Methods**

### **Introduction**

In order to address the aims of this thesis, I have used two samples that complement each other. These samples are used in the following chapters, with different sub-samples being included to answer different questions. Both samples are from longitudinal studies of children and adolescents in the United Kingdom. This chapter includes a description of the samples, procedures and measures of each of the studies, leaving the specific details of the relevant sub-samples to be briefly described in subsequent chapters. The first study I will describe is the Cardiff Study of All Wales and North West of England Twins (CaStANET) which is both longitudinal and genetically sensitive. The second study I will describe is the South Wales Family Study (SWFS) which is also a longitudinal study. Once the samples, measures and procedures of both of these studies have been described I will describe the methods of analyses used within subsequent chapters of this thesis. This will include a description of the twin methodology and model fitting strategy, followed by a description of the longitudinal cross lagged panel analysis.

The data for both of these samples had already been collected when I began my research for this thesis. Prior to beginning my research however, I was involved with the collection of the CaStANET sample data as part of my employment. My position as Research Technician meant that I assisted my colleagues with compiling the questionnaires and preparing documentation for amendments to the MREC for the CaStANET study in 2004. I was responsible for maintaining the Twin Register, mailing the questionnaires, entering the data and assisting with the supervision of data entry. I was not instrumental in deciding which measures were included in the

questionnaires for either study. During my studies for this thesis however I had access to the raw data from both samples from which I computed the composite scores on each of the scales. I used these composites for my analyses.

## **Cardiff Study of All Wales and North West of England Twins**

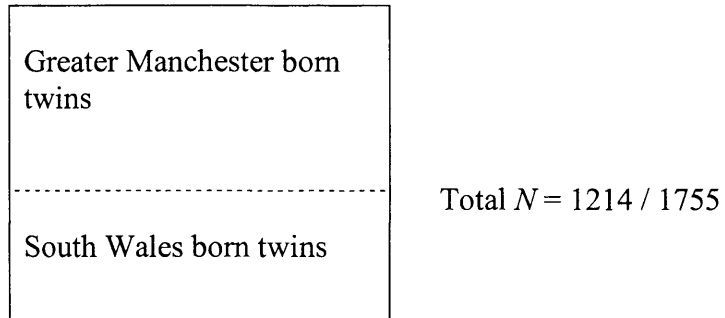
### *Sample*

The first sample included twins and their families who were on the CaStANET register. This is a population based register which is housed at Cardiff University and has been utilised for a number of studies (see van den Bree et al., 2007). Twins who were born in South Wales and Greater Manchester were systematically obtained from birth register records. Families have been contacted on a number of occasions to invite them to take part in research studies. The main sample used for this thesis is from families who participated in the 2004 study on Health, Habits and Behaviour. Ethical approval was obtained from the Multi-Centre Research Ethics Committee (MREC) for Wales for this wave of data collection (MREC reference 98/9/20). In total there were 1214 families where at least one family member took part in this study out of 1755 families contacted (response rate 69%; Figure 2.1). Twins were aged between 11 and 20 years of age ( $M = 16.14$ ,  $SD = 1.94$ ). The sample included information on 468 monozygotic (MZ) twin pairs (203 male pairs and 265 female pairs) and 724 dizygotic (DZ) twin pairs (161 male pairs, 194 female pairs and 369 opposite sex pairs). Zygosity information was missing for 22 pairs (12 male pairs and 9 female pairs). Seventy eight percent (78%) of the sample were from two parent families.

CaStANET 2004 data collection

Aged 11 to 20 years old

DOB 1991 to 1985

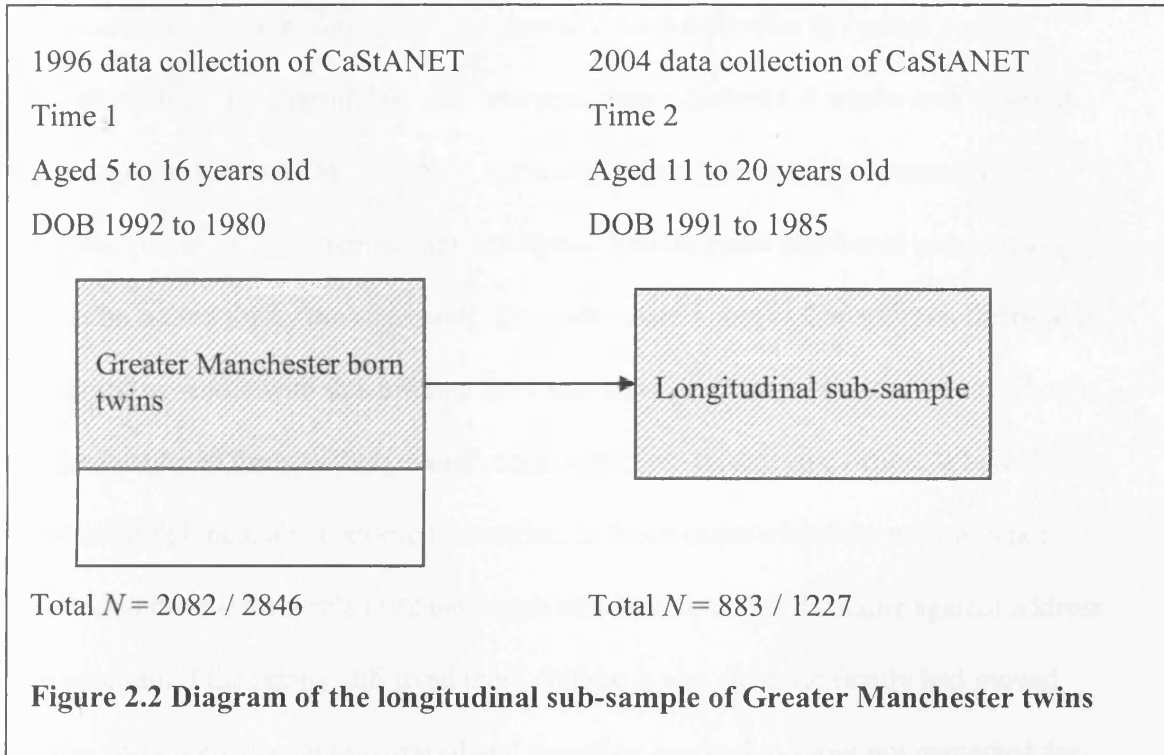


**Figure 2.1 Total sample of twins taking part in CaStANET in 2004. The sample includes those from the Greater Manchester Twin Register and the South Wales Twin Register.**

### *Longitudinal sub-sample*

At a previous data collection point of CaStANET (in 1996) 2082 families had taken part (73% response rate). Ethical approval had been granted from the appropriate Local Research Ethics Committees (LREC) within the Greater Manchester area for this previous data collection point. Of the 2082 families who previously took part, only 1227 were contacted in 2004. Longitudinal data were available for a sub-sample of 833 families who took part at both time points (Figure 2.2). These two data collection points (1996 and 2004) of CaStANET were selected for use because this was when ADHD data was most completely collected. The sub-sample included 313 MZ twin pairs (143 male pairs and 170 female pairs), 503 DZ twin pairs (105 male pairs, 147 female pairs and 251 opposite sex pairs) and 17 pairs with no zygosity information (11 male pairs and 6 female pairs). At the initial time point (Time 1) twins were aged between 5 and 15 years of age ( $M = 9.20$ ,  $SD = 1.89$ ). Those who were eligible to take part at both time points but only took part in at Time 1 were compared to those who took part at both time points. Those who only took part at Time 1 were significantly older ( $M = 9.5$  years,  $SD = 1.92$ ) than those who also took part in 2004 (Time 2;  $M = 9.2$  years,  $SD = 1.89$ ,  $t_{(1375)} = 3.26$ ,  $p = .001$ ). A greater proportion of boys (53%) took part only at Time 1 compared with the proportion that took part at both time points (47%). Gender significantly predicted participation status, with females being more likely to take part at both time points than males (OR 1.3, 95% Confidence Interval (CI) = 1.09 to 1.58). Also, those who only took part at Time 1 showed slightly greater ADHD symptom scores ( $M = 13.77$ ,  $SE = .41$ ) than those who took part at both time points ( $M = 12.31$ ,  $SE = .31$ ,  $t_{(1375)} = 2.83$ ,  $p < .01$ ). This may be accounted for by the fact that a greater proportion of boys were included at the earlier time point, hence ADHD symptom scores would be

expected to be somewhat higher. However, they were also slightly older, and this would perhaps lead the scores to be lower since ADHD symptoms tend to decrease with age.



### *Procedure*

In the main study (Time 2, 2004 data collection point) parents and their twins were sent questionnaires with a letter explaining the study and asking if they would like to take part. Parents were initially mailed the questionnaires and it was explained that the researchers would also be contacting their twins a few days later with a similar questionnaire. A free-phone number was given for further information or to request a questionnaire in Welsh. Completing the questionnaire was taken as consent to take part. A tick box was included on both the invitation letter and questionnaire for participants to indicate if they did not want to take part. Participants were asked to

tick this box and return the blank questionnaire if they did not want to take part and reminders were then not sent to these individuals. Mothers were asked to complete the parent questionnaire in order to remain consistent with previous data collection points. Non-responders were sent postcards and reminder questionnaires and letters. Postcards were sent to families approximately 4-6 weeks after the initial mail. A questionnaire with a reminder letter was sent after a further 4-6 weeks and was sent registered post if none of the family members had replied in order to ascertain whether the family still resided at the address. Sending post registered means that it must be signed for by the addressee. If the addressee is not at that address, the mail is returned to sender with this information detailed on it. If the addressee is not at home, a card is placed through their door to collect the post from a post office. Where this is not collected the mail is returned to sender. In those cases where the mail was not collected the electoral role (192 database) was used to check the name against address to ascertain if the family still lived there. Where it was clear the family had moved, these cases were deemed not traced and therefore counted as those not contacted for the study. After the registered mail, another reminder postcard was sent at 8 weeks and then a final reminder letter after a further 3 weeks. Each participant was sent a £5 gift voucher for high street stores on completion of the questionnaires as a way of thanking them for participating.

#### *Longitudinal sub-sample previous data collection procedure*

During the earlier data collection point for the sub-sample of twins born in Greater Manchester, none of the twins completed questionnaires themselves, just the parents. Again it was requested that the mother complete the questionnaire where possible. Non-responding parents were sent a reminder postcard followed by another

questionnaire with reminder cover sheet if they still did not respond. Completing the questionnaire was taken as consent to take part.

### *Measures*

#### *Twin zygosity*

Zygosity was assigned on the basis of a twin similarity questionnaire (Cohen, Dibble, Grawe & Pollin, 1975; Nichols & Bilbro, 1966) included in the parent questionnaire at previous data collection points (Time 1; Appendix I). This has been shown to correctly assign zygosity at over 90% (Scourfield, Martin, Lewis & McGuffin, 1999; Thapar, Harrington, Ross & McGuffin, 2000). Where there was missing data from Time 1, zygosity at from an interim data collection point (in 2000) was used. Where there were discrepancies these were resolved at the interim collection point and hence the zygosity information from this wave was used where necessary.

#### *ADHD symptoms*

ADHD symptoms were measured using the DuPaul rating scale (DuPaul, 1991) which is based on DSM-III-R criteria for ADHD. Four extra items were included to cover DSM-IV symptoms and this overall measure has previously been used and validated (Appendix II; Thapar et al., 2000). Mothers were asked to report on their children's behaviour during the past 3 months. The items included those on inattention (9 items), overactivity (4 items) and impulsivity (5 items). The overall scale therefore included 18 items each rated on a 4-point likert scale ranging from "not at all" (scored 0) to "very much" (scored 3), thus the scale scores ranged between 0 and 54. Internal consistency for the scale was good (Time 1  $\alpha = .94$ , Time 2  $\alpha =$



.94). The DuPaul scale may be less susceptible to rater bias than other measures of ADHD because models which include non-additive genetic effects rather than rater contrast effect have been shown to fit ADHD symptoms data using the DuPaul measure (Thapar et al., 2000).

Parent reports of their children's ADHD were used rather than self reports. When comparing parent and self reports of ADHD symptoms Barkley, Fischer, Smallish and Fletcher (2002) showed that symptoms counts were not significantly correlated. Also, for diagnosis of ADHD, of those rated high by the parent only 10% were also reported high for the self-report suggesting that using self report misses a substantial proportion of those with ADHD compared with parent report (Barkley et al., 2002). When assessing which reporter may be more useful to use, parent report was found to be associated with more outcomes (of ADHD) such as education, performance at work and number of arrests and thus deemed more useful (Barkley et al., 2002).

#### *Parent-child warmth and hostility*

Measures of warmth and hostility were also included in the questionnaires sent out at Time 2 (Appendix III). For these measures twins were asked to complete a set of 10 questions regarding the quality of their relationship with their mother (or the person who was most like a mother to them), and then complete the same set of questions regarding their relationship quality with their father (or the person most like a father to them). Participants were asked to rate how often their mother/father displayed particular behaviours during the past month when spending time with them. Responses were completed using a 7 point likert scale ranging from 1 "never" to 7 "always". Five items load onto the hostility subscale and 5 onto the warmth subscale.

These were based on questions from the Iowa Youth and Family Project (IYFP; Melby et al., 1993). The warmth scale included items such as “let you know s/he really cares about you” and “help you do something that was important to you”. The hostility scale included items such as “get angry at you” and “get into an argument with you”. Internal consistency was good for both parent-child warmth (range  $\alpha = .92$  to  $.93$ ) and parent-child hostility (range  $\alpha = .88$  to  $.90$ ). These measures had not been included at the previous data collection (Time 1) and thus there are no longitudinal twin data for these measures.

### *Family conflict*

One of the questionnaires in the booklet sent to twins’ parents comprised of some of the items from the Family Environment Scale (FES; Moos & Moos, 1976). The FES is a measure of social climate within the family (Touliatos, Perlmutter & Straus, 2001). The full scale includes ten subscales, however in the present study a nine item version was used to measure family conflict (Appendix II). The questionnaire included items such as “we fight a lot in our family” and “family members often criticise one another”. Parents were asked to rate the items as strongly disagree, disagree, agree and strongly agree. To conform to the standardised FES, these were then recoded so that strongly disagree and disagree were ‘false’ and agree or strongly agree were ‘true’. False was coded as 0 and true as 1 except in the cases where items were worded to be low in conflict where the scoring was reversed to be false = 1 and true = 0. Scores were then summed across the 9 items and the resulting scale therefore ranges from 0 to 9 with a score of 9 representing high family conflict. The internal consistency of the scale was  $\alpha = .73$  and  $\alpha = .75$  at Time 1 and Time 2 respectively.

### *Associations between Family Relationship Factors*

Correlations between the family relationship variables were moderate, suggesting that they measure different constructs. The parent-child warmth variables were inverse transformed to correct for skewness, therefore high scores on the warmth variable reflect low levels of warmth. Family conflict showed low to moderate correlations with parent-child warmth ( $r = .21, r = .22, p < .01$ ) and parent-child hostility ( $r = .33, r = .34, p < .01$ ). Parent-child warmth and hostility were also moderately correlated (range  $r = .31$  to  $.48, p < .01$ ).

### **Use of Twin Sample**

Both the whole CaStANET sample (Time 2, 2004) and the longitudinal sub-sample (Time 1 and Time 2) are used in the next chapter (Chapter 3) to examine the genetic and environmental influences on ADHD and its continuation. The dataset from Time 2 is also used in Chapter 4 to address the genetic and environmental influences on the association between ADHD symptoms and specific dimensions of parent-child relationships. In Chapter 5 the CaStANET longitudinal sub-sample is used to examine the direction of effects between ADHD symptoms and family conflict.

### **South Wales Family Study**

#### *Sample*

The second sample consisted of children and their parents who took part in the SWFS. This is a three year longitudinal community study including families with

children at nine different schools in South Wales. Ethical approval for this study was obtained in 1999 from the School of Psychology Ethics Committee at Cardiff University. In total, 543 families consented to take part out of 652 approached, therefore giving a response rate of 83%. 543 children (aged 11 to 13 years old) and 387 parents (at least one parent from a family) initially took part. At Time 2, 496 children (aged 12 to 14 years old) and 318 parents (at least one parent from a family) completed questionnaires. For the analyses in this thesis only those families where the child and at least one parent took part at Time 1 and Time 2 were included and therefore the sample size was 309 families (there were 9 cases at Time 2 where the parent replied at but the child did not). The vast majority of children in the sample (92%) were from two parent families. Comparing the children in the 309 sample with those who took part at Time 1, ADHD symptoms reported by the mother were significantly greater in those who only took part at Time 1 ( $M = 5.28$ ,  $SD = 4.48$ ) than those who were included at both time points ( $M = 3.56$ ,  $SD = 3.34$ ,  $t_{(100.12)} = 3.17$ ,  $p < .01$ ). Using father reports of ADHD symptoms there was no difference in mean between the two groups (Time 1 only  $M = 4.58$ ,  $SD = 4.62$ , both time points  $M = 3.55$ ,  $SD = 3.19$ ,  $t_{(72.16)} = 1.65$ ,  $p = .10$ ). A slightly greater proportion of females were included in the main sample ( $157/309 = 50.8\%$ ) than in those who were not ( $107/234 = 45.7\%$ ) however gender did not significantly predict being in the main sample (OR = 1.2, 95% CI .87 to 1.72).

### *Procedure*

Schools were approached to take part in the study based on the demographics in their catchment area (that is, the area from which children are eligible to attend the school). This was done to ensure a diverse sample which was representative of

schools in South Wales. Demographic information on the families in the overall study sample confirmed that it was representative of families living in England and Wales in terms of family composition, parent education and ethnic representation (Harold & Honess, 2001). After schools ( $n = 9$ ) had agreed to take part in the research, parents were sent a letter giving them details of the study and inviting them to take part. During parent-teacher meetings the team of researchers gave a presentation about the study and each of its stages. A letter with further information regarding the goals and each stage of the study and a consent form to participate were also given to the parents. The children whose parents had consented to take part were asked to complete a questionnaire during part of the school day when the researchers visited. Parents were then also mailed questionnaires for them to complete along with instructions on how to complete them and a pre-paid envelope to reply. Both mothers and fathers were asked to complete questionnaires which were identical and they were asked to complete them independently. The questionnaires included a range of questions asking about their child's health and behaviour, their relationship with their child and with their spouse/partner as well as a range of socio-demographic information.

Families who took part were sent questionnaires three times, at yearly intervals (data from the first two years are used for this thesis). In between each data collection point families were sent a Christmas card along with a letter to thank them for participating and to inform them of what was going to happen next in the study. They were also given the contact details for the principle investigator both at the times of taking part and in the annual Christmas letter in case they had any concerns or questions. At the end of the study, those who had taken part in the whole study were sent a book about how conflict between parents affects children.

## *Measures*

### *ADHD symptoms*

The attention problems subscale of the Child Behavior Checklist (CBCL; Achenbach, 1991) was used as the measure of ADHD in this study (Appendix IV). The subscale consists of 11 items which include those on inattention, impulsivity and overactivity. Parents were asked to report on their child's behaviour over the past six months. Each item was scored on a three point likert scale of 0 = not true, 1 = sometimes true, 2 = very true. These items were then summed to obtain an overall ADHD score which potentially ranged from 0 to 22. Both mothers and fathers reported on their child's ADHD symptoms. Internal consistency was good for both mother and father reports of attention problems ( $\alpha = .80$  to  $.81$ ).

The CBCL is a widely used instrument used to assess children's emotional and behavioural problems/adjustment. Frequently the externalising composite, which includes the delinquent and aggressive subscales but not the attention problems subscale, has been used as an outcome measure in developmental research (e.g. when examining the influence of parent-child relationship, or inter-parental relationship on child adjustment). The attention problems subscale has been shown to be an effective screening tool for ADHD and the best predictor of ADHD out of all of the CBCL subscales (Chen, Faraone, Biederman & Tsuang, 1994). Associations between the attention problem subscale and other measures of ADHD have also been shown to be good (Derks et al., 2008).

### *Parent-child hostility, warmth and rejection*

The IYFP instrument which measures warmth and hostility was also completed by children (Appendix V). These measures included the same items as in the twin study. Internal consistency was good for parent-child warmth (range  $\alpha = .83$  to  $.90$ ) and hostility (range  $\alpha = .80$  to  $.90$ ).

Children also completed items from the Children's Report of Parental Behavior Inventory (CRPBI; Schaefer, 1965). This includes a number of subscales, however the rejection (7 items) and acceptance (8 items) subscales were used in the current study (Appendix V). These both load onto the acceptance vs. rejection factor of the Inventory. Rejection was reverse coded to form the composite with acceptance. Items such as "seems proud of the things I do" (acceptance item) and "isn't very patient with me" (rejection item) were responded to on a 3 point likert scale of true (1), sort of true (2) and not true (3). These were then summed so that the overall scale potentially ranged between 15 and 45. The overall composite of the acceptance and rejection subscales is termed rejection as high scores indicate high rejection and low scores indicate low rejection (and high acceptance). Children reported both on their relationship with their mother and then separately reported on their relationship with their father. The rejection subscale showed good internal consistency for mother and father-child rejection (range  $\alpha = .87$  to  $.91$ ).

### *Family conflict*

Family conflict was also measured using the conflict subscale of the FES (Moos & Moos, 1976) as in the twin sample. In the SWFS however it was the children who completed this scale rather than the parents (Appendix V). Children were instructed to think if the statements were true (or mostly true) or false (or mostly

false) for their family and then asked to rate the items accordingly as true or false. Two items were different in this study compared with the CaStANET questionnaire. “Family member sometimes really lose their temper” was in the SWFS whereas the CaStANET questionnaire item was “family members sometimes get so angry they throw things”, also “family members sometimes really shout at each other” was in this study (SWFS) compared with “family members sometimes hit each other” which was in the CaStANET questionnaire. Even with these different items the internal consistency was still reasonable ( $\alpha = .68$  to  $.73$ ).

#### *Associations between Family Relationship Factors*

Correlations were computed between the family relationship variables. Scales which were not approximately normal were transformed. This included using an inverse transformation for the warmth variables and therefore a high score represents low warmth. Family conflict and hostility in the parent-child relationship within time points were moderately correlated ( $r = .33$  to  $.48, p < .01$ ), similarly family conflict and parent-child warmth were correlated but to a lesser degree ( $r = .28$  to  $.38, p < .01$ ). Family conflict was moderately correlated with rejection in the parent-child relationship ( $r = .44$  to  $.48, p < .01$ ). Parent-child hostility and rejection showed moderate to strong correlations within time ( $r = .35$  to  $.67, p < .01$ ). Parent-child warmth also showed moderate to strong correlations with parent-child rejection ( $r = .34$  to  $.66, p < .01$ ) and with parent-child hostility ( $r = .28$  to  $.54, p < .01$ ). These moderate correlations between many of the family relationship variables suggest that while the different aspects of family relationships are associated with each other the measures are assessing distinct aspects of family relationships.



## **Use of SWFS Sample**

The SWFS sample is used in Chapter 4 to assess the directional nature of the association between ADHD symptoms and parent-child hostility for both girls and boys separately. In Chapter 5 this study is used to examine the longitudinal association between ADHD symptoms and family conflict as well as rejection in the parent-child relationship.

## **Twin Analyses**

This section includes descriptions of the analyses used in the subsequent chapters. Firstly, I will give a summary of the twin methodology followed by a description of the model fitting strategy used for both univariate and bivariate genetic analyses. Details of assessing the fit of a twin model will next be described. Then I shall describe the method of assessing MZ twin differences to test whether the association between family relationship factors and ADHD symptoms are due to non-shared environmental influences on both variables.

### *Twin Methodology*

The twin methodology is based on the principle that MZ twins share all of their genes in common whereas DZ twins share on average half of their genes (like other biological siblings). Using this information the overall variation in a trait can be decomposed into additive genetic (A), non-additive genetic (D), shared environmental (C) and non-shared environmental (E) influences. This can be represented mathematically by the following formulae (Neale & Cardon, 1992)

$$V_p = a^2 + d^2 + c^2 + e^2$$

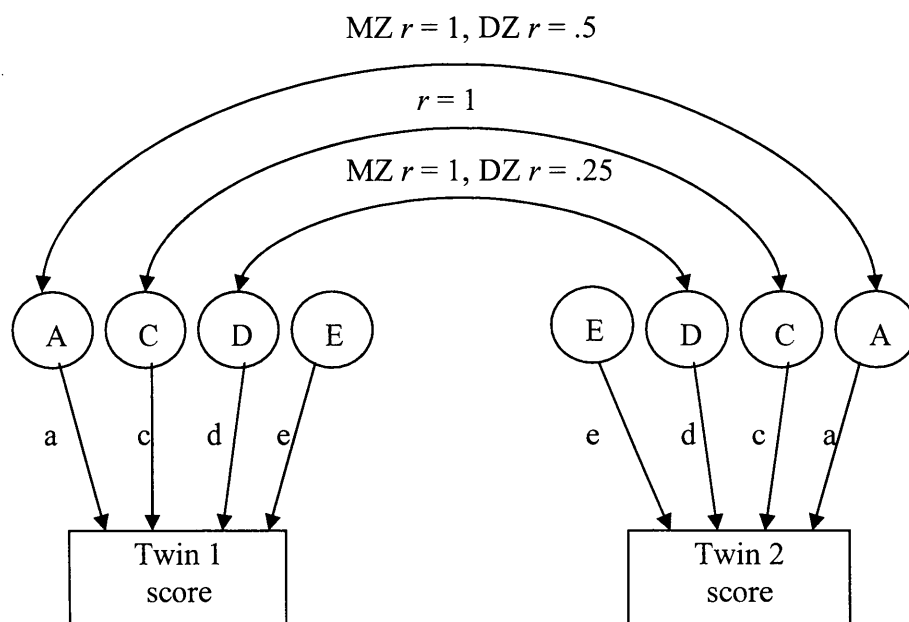
Where  $V_p$  is the variance of the trait,  $a^2$  is the additive genetic path coefficient,  $d^2$  is the non-additive genetic path coefficient,  $c^2$  is the shared environmental path coefficient and  $e^2$  is the non-shared environmental path coefficient.

Because of the differential relatedness of MZ and DZ twins, the covariance between twins (reared together) on a given trait is

$$\text{Cov MZ} = a^2 + d^2 + c^2$$

$$\text{Cov DZ} = \frac{1}{2} a^2 + \frac{1}{4} d^2 + c^2$$

These formulae can be seen by tracing the pathways in the diagram (Figure 2.3). MZ twins share all of their genes in common, thus the correlation between additive genetic and non-additive genetic influences is 1. However for DZ twins who share on average half of their genes in common with their cotwin (like other siblings), the correlation between additive genetic influences is therefore .5 and for non-additive genetic factors is .25. Shared environmental influences are necessarily shared between twins as these are influences which make twins more similar to each other (as opposed to literally just environmental influences which are shared between the two). Non-shared environmental influences however are those which make twins more dissimilar from each other and therefore do not account for any of the covariance of a trait between twins.



**Figure 2.3 Path diagram of the twin model**

*Assessing heritability*

The heritability of a trait is the amount of variation of the trait which is due to genetic influences. Broad heritability ( $h^2$ ), that is variation due to both additive and non-additive genetic influences, can be assessed using the twin correlations. That is:

$$h^2 = 2(r_{MZ} - r_{DZ})$$

Estimates of environmental influences can also be calculated using the MZ and DZ twin correlations:

$$c^2 = r_{MZ} - h^2$$

$$e^2 = 1 - r_{MZ}$$

These formulae can therefore give an idea of what proportion of the variance these factors account for.

Examining the pattern of MZ and DZ correlations can give an indication as to which factors are influencing a trait. Where the correlation between DZ twins is less than for MZ twins genetic factors are expected to contribute. Where the DZ

correlation is half that of the MZ correlation, additive genetic factors are suggested. Shared environmental and non-additive genetic factors have differing effects on the correlations between MZ and DZ twins. Shared environmental effects make twins more similar than would be expected purely based on their genetic relatedness and therefore the DZ correlation is more similar to the MZ twin correlation (i.e. the DZ correlation is greater than half the MZ correlation). Non-additive genetic effects however make DZ twin correlations more dissimilar to MZ twin correlations (i.e. the DZ correlation is less than half the MZ correlation). Shared environmental and non-additive genetic influences may both have an impact on a trait, but using a twin design only there is not enough information from MZ and DZ twins to estimate both parameters (i.e.  $c^2$  and  $d^2$ ). A choice must therefore be made as to which is model is expected to explain the data. Comparison of the correlation coefficients for MZ and DZ twins along with previous research evidence should guide the expected and tested twin model.

### *Testing for gender effects*

Where the pattern of twin correlations is similar for males and females but the magnitudes of the correlations differ, this indicates that there may be quantitative gender differences. That is, the same genetic and environmental factors may be influencing the trait for both males and females but the proportion of the variance attributed to each factor may vary by gender. Alternatively, another pattern of correlations may suggest a different genetic architecture of the trait for males and females. This is suggested when for example the correlations for males suggest an ACE model but the correlations for females suggest an ADE model. Another type of gender difference is suggested when the opposite sex DZ twin correlation is lower

than the same sex DZ twin correlation. This pattern suggests that different genes may be affecting males and females, thus suggesting qualitative gender differences in genetic aetiology.

### *Twin assumptions*

The twin methodology is not only based on the genetic relatedness of MZ and DZ twins, but also on the assumption that MZ and DZ twins share to the same extent the environments which are important to the trait being measured. This is why MZ twins are compared with DZ twins rather than just comparing MZ twins with siblings, who are genetically as similar as DZ twins but who may not share such similar environments. Violation of this assumption of equal environments becomes a problem when MZ and DZ twins do not share environments to the same extent and this has an impact upon the trait or disorder of interest. Where this is the case the estimate of genetic influence may be over or under estimated (Rutter, 2006). In the case where there is evidence for genetic influence on an environmental factor (i.e. gene-environment correlation,  $r_{GE}$ , as described in the Introduction Chapter) and this environmental factor has an impact upon the disorder or trait of interest, the equal environments assumption is therefore violated to some extent (Rutter, 2006). Within the classic twin design the heritability of the trait is therefore overestimated because the effect of  $r_{GE}$  is included in the heritability estimate (Rutter, 2006).

There is also an underlying assumption that twins are comparable to singletons on the traits being examined. This is important so that results may be generalised to singletons. While this does generally seem to be the case, there are a few differences between twins and singletons. Firstly, mothers have more obstetric complications when having a multiple pregnancy (Rutter, Thorpe, Greenwood, Northstone &

Golding, 2003; Rutter, 2006). Secondly, twins tend to have more language delays than singletons, with an estimated delay of 3 months at age 3 years old (Rutter et al., 2003).

### *Model Fitting Strategy*

#### *Univariate genetic analyses*

In this thesis twin correlations were calculated and examined. Models were then hypothesised and fitted to the data accordingly. The statistical package Mx (Neale, Boker, Xie & Maes, 1999) was used to test models and estimate the amount of influence genetic and environmental factors have on the measure being examined using observed data from MZ and DZ twins. Raw data files which include missing data were used as these can be analysed by Mx and maximise the data used.

*Estimating means, variances and covariance.* Initially a saturated model was fitted to the data which estimated means, variances, covariances and the effects of covariates (e.g. age) for the trait. This was followed by fitting a series of models which tested for twin order and zygosity influences on means, variances and covariances. These models fixed the means, variances or covariances to be equal across gender, zygosity or twin order. The changes in model fit were assessed. The effects of chosen covariates were also tested by including them in the initial saturated model and then dropping their estimated effect and assessing the change in model fit. Next genetic model fitting was undertaken. These subsequent models were compared with the full saturated model (with covariates included as appropriate) in order to assess the fit of each model (see assessing model fit section below for more details).

*Testing for gender effects.* First, a series of univariate genetic models that allow for differences between genders were fitted to the data. This allowed for the possibility that there may be gender differences and this needed to be undertaken before fitting models which included both males and females that assumed they are equal. The models used were heterogeneity models which allow for differences between genders. These models (also known as sex-limitation models) were fit to the data using Mx scripts based on those found in the Mx scripts library ([www.psy.vu.nl/mxbib/index.php?page=home](http://www.psy.vu.nl/mxbib/index.php?page=home)) where initially the parameter estimates for males and females were allowed to differ, followed by constraining them to be equal in later models. First, a full genetic model was fitted to the data. This allowed each parameter estimate (e.g. A, D, E) to vary for males and females as well as the correlation of additive genetic influences between opposite sex twins to be less than 0.5. This therefore models gender differences in the magnitude of genetic and environmental influences (i.e. quantitative gender differences) as well as qualitative differences in additive genetic influence (i.e. different genes are important for males and females). In cases where it was appropriate to begin with an ADE model rather than an ACE model, another full genetic model was also fitted which allowed each parameter to vary by gender but this time the correlation between non-additive genetic influences between opposite sex twins was allowed to be less than 0.25 (but the additive genetic correlation to must be fixed to 0.5), thus modelling different non-additive genetic effects in males and females. Next, a common gender effects model which constrains the opposite sex correlation of genetic influences (both additive and non-additive where appropriate) to equal that of same sex DZ twins was fitted to test whether the same genes are important for males and females. The common gender effects model therefore constrains the opposite sex twin correlation between A for

males and females to be 0.5 and between D for males and females to be 0.25. In this model qualitative gender differences are not included but because the estimates for the parameters (e.g. A, D & E) are allowed to vary in the models there may be quantitative gender differences i.e. a different amount of variance being explained by each factor for males and females. Hence the same genetic factors on the trait are fixed to be the same for males and females (which is why this is described as a common gender effects model) even though the extent to which they explain the trait for each gender is allowed to differ. Following this, a no gender effects model was fit to the data where all parameter estimates for males and females are constrained to be equal thus modelling no gender differences.

Where correlations suggested different models for males and females (for example ACE for females but ADE for males), models which accounted for these differences were fitted to the data. Where there were significant differences in variances for males and females a scalar effects model was fitted. This constrained the standardised parameter estimates for males and females to be equal using a scalar function, but allowed the variances for males and females to differ and therefore the unstandardised components to differ (Neale & Cardon, 1992).

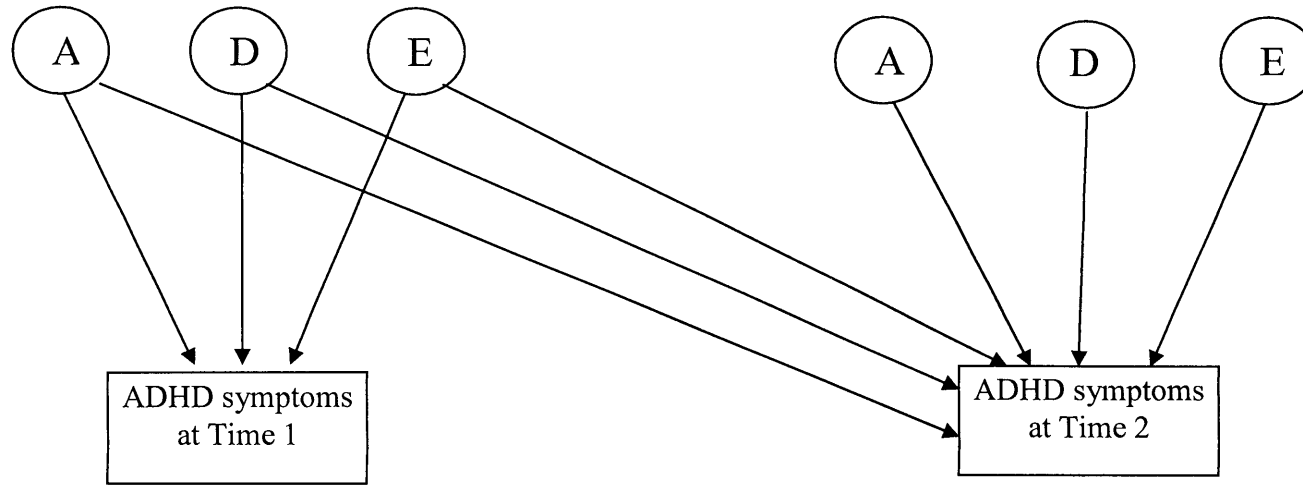
*Testing different genetic models.* Once it was established whether or not there were gender effects, the appropriate model (i.e. a model either including gender differences where they were significant, or not including gender differences where they were not significant) was then used as the full model (e.g. ACE or ADE). Nested models where parameters were dropped were then compared with the full model and change in model fit was examined to assess which was the most parsimonious explanation of the data. Finally, where contrast effects were suggested by differing



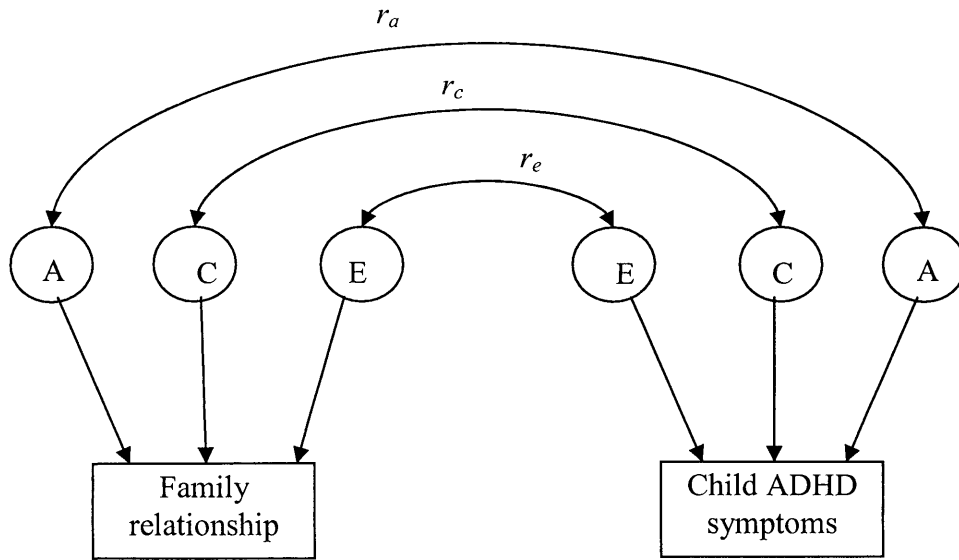
variances between MZ and DZ twins as well as a DZ twin correlation which was less than half that of the MZ twins, a model which incorporated these effects was fitted to the data.

### *Bivariate genetic analyses*

Bivariate genetic analysis was used to examine the influence of genetic and environmental factors on the relationship between two variables (family relationship factor and ADHD symptoms; ADHD symptoms at two time points). A Cholesky decomposition model (Figure 2.4) was used to assess the relationship of the same variables across time (as with ADHD symptoms at both time points in Chapter 3). A correlated factors model (Figure 2.5) was used to assess the relationship of two variables within time (as with ADHD symptoms and family variables in Chapter 4). Similar to the univariate analyses, an initial saturated bivariate model which modelled the means, variances and covariances was fitted to the data. In each situation accepted univariate models were used to inform the parameters included in the bivariate models. Cross-twin cross-trait correlations were also used to inform the expected bivariate models. The covariates which were significant within the univariate models were also included on each specific variable. Gender differences were also tested within the bivariate models. Having established whether gender differences were apparent, parameters were then dropped in nested models and change in model fit was assessed.



**Figure 2.4 Cholesky model, example of ADE model**



**Figure 2.5 Correlated factors model, example of ACE model**

### *Assessing Genetic Model Fit*

As described in Neale and Cardon (1992) a good model should be judged on four criteria, its fit, consistency, simplicity and significance of the parameter estimates. When using raw data, model fit can be assessed by comparing the minus two times the log likelihood (-2LL) of a model with the -2LL of a saturated model which estimates means, variances and covariances of the raw data (Koenen, Moffitt, Caspi, Taylor & Purcell, 2003). The difference in -2LL is interpreted as a  $\chi^2$  statistic, with the degrees of freedom equalling the difference between those in the test model and those in the saturated model (Koenen et al., 2003). The Akaike's Information Criterion (AIC) is another fit index which assesses parsimony as well as goodness of fit (it is a function of the  $\chi^2$  and df) and is therefore useful to use as well as the  $\chi^2$  statistic (see Neiderhiser, Reiss, Lichtenstein, Spotts & Ganiban, 2007). The AIC is calculated by subtracting twice the degrees of freedom from the  $\chi^2$  of a model (that is  $AIC = \Delta-2LL - 2\Delta df$ ; Haberstick et al., 2008; Neale & Cardon, 1992). The  $\chi^2$  statistic and AIC give an assessment of the fit of the model (against the saturated model) with a non-significant  $\chi^2$  and a low (and negative) AIC representing a good fit. It is conventional (Kim-Cohen, Moffitt, Caspi & Taylor, 2004; Kuntsi et al., 2005; McLoughlin, Ronald, Kuntsi, Asherson & Plomin, 2007; Polderman et al., 2007; Rietveld et al., 2004; Simonoff et al., 1998; Wood, Saudino, Rogers, Asherson & Kuntsi, 2007; Wood, Rijdsdijk, Saudino, Asherson & Kuntsi, 2008) to compare nested models (e.g. ACE with AE) by examining the difference between the  $\chi^2$  of each model along with the difference in degrees of freedom. Where there is no significant difference between the models, the model with the least parameters (i.e. the nested model) is considered the most acceptable as it is the more parsimonious and there has been no significant reduction in model fit (Koenen et al., 2003; Polderman et al.,

2007). Where there is more than one model which does not differ based on the  $\chi^2$  test or where models are not nested, the AIC is used to establish the accepted model, with the model with the lowest AIC providing the better fit (McLoughlin et al., 2007; Wood et al., 2008). Along with these fit statistics the confidence intervals around each parameter estimate are also examined. Non-significant parameters suggest the model is a poor fit to the data.

*Testing Whether the Association between Two Variables is due to Genetic or Environmental Factors*

The extent to which the association between two variables is due to genetic and environmental factors can be tested using bivariate genetic analysis as previously described. Another method to assess environmental mediation is to examine the association between differences in MZ twin ADHD scores and differences in their family relationship dimension scores. This examines the non-shared environmental influences which are shared between the two variables. Anything less than a perfect correlation between MZ twins is attributed to non-shared environmental influences (plus measurement error) because any difference between them must be due to environmental factors which make them more dissimilar to each other as they are genetically identical. Therefore correlating the difference scores on two variables gives an estimate of the relationship between non-shared environmental influences on each variable (i.e. a positive correlation would indicate that things that make twins differ on one variable also make them differ on another). The differences in transformed scores were computed to account for kurtosis in the difference score distributions. The relationship between difference scores was then assessed using correlational analyses with age and gender included as covariates where appropriate.

Where gender differences were suggested from the univariate analyses and the bivariate analyses, the MZ difference correlations were computed for each gender separately (and only age was included as a covariate).

### **Longitudinal Data Analyses**

In this section the path analysis used for the longitudinal data analysis assessing the direction of effects will be described.

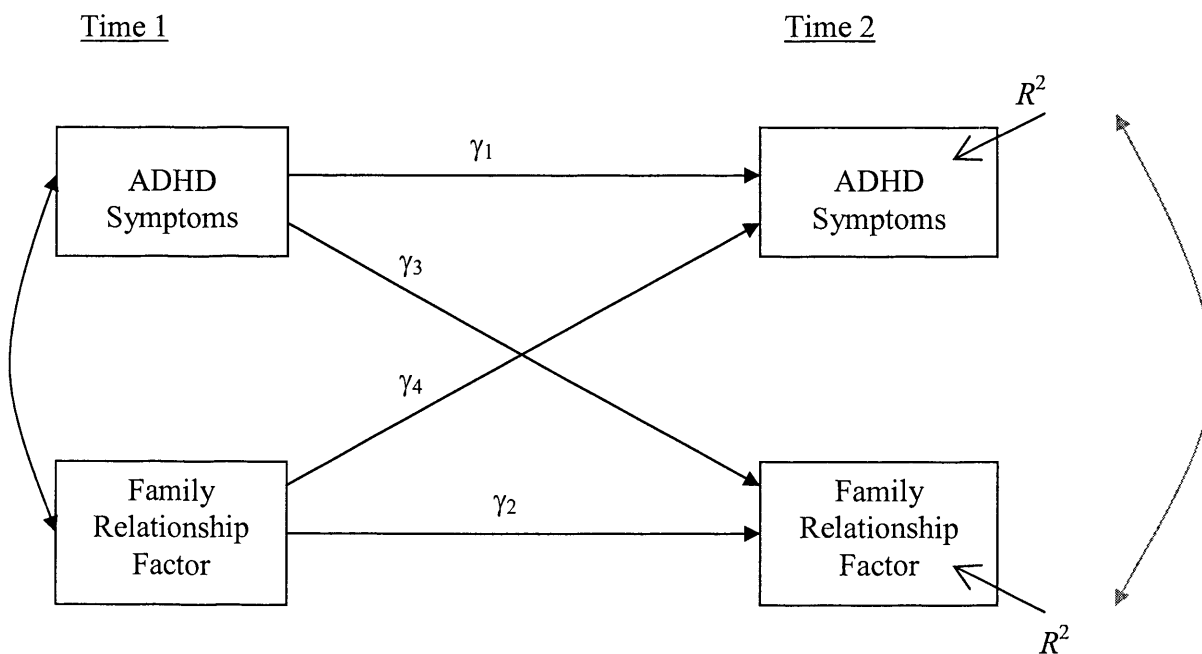
#### *Assessing the Direction of Effects: Cross Lagged Panel Analysis*

To assess the direction of effects between ADHD symptoms and different family relationship dimensions cross lagged panel analyses were used. Initial correlations between variables within and across time were computed. Where there were no significant correlations between the two variables, or where the only significant correlation between variables was at Time 1, no further analyses were carried out. However, where there were significant correlations between variables across time and/or within time at Time 2, path analysis was used to examine the association between the two variables. Whereas multiple regression includes one dependent (predicted) variable and one or more independent (predictor) variables, path analyses is an extension of this where the relationships between a number of variables can be simultaneous estimated.

#### *Assessing change across time*

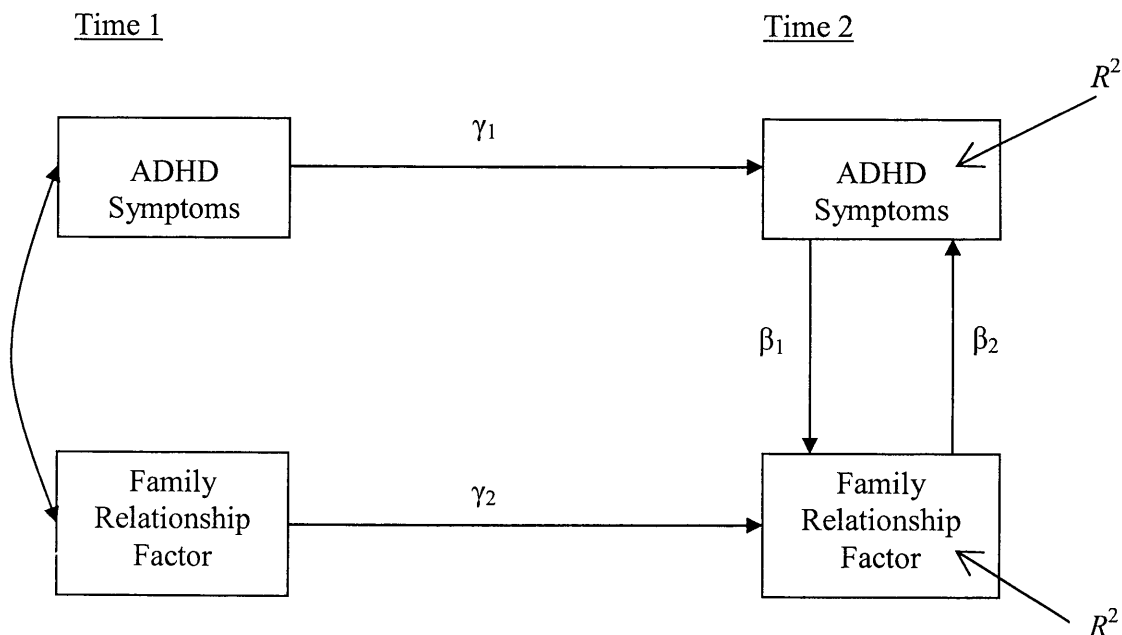
To assess the relationship between ADHD symptoms and family relationships over time path analyses were conducted using LISREL (LISREL 8.80; Jöreskog & Sörbom, 2006). Specifically, cross lagged panel analysis and reciprocal effects

models were estimated. Using these models it was possible to assess the impact of each variable of interest on another whilst controlling for previous levels of each. The amount of explained variance in each variable at Time 2 is computed within these models. The cross lagged panel model (Figure 2.6) assess the relationship across time, that is the impact of Time 1 ADHD symptoms on family relationship measure at Time 2 and vice versa (pathways  $\gamma_3$  and  $\gamma_4$  in Figure 2.6). Because in this example initial (i.e. Time 1) level of family relationship measure is included in the model, any variation that ADHD symptoms are explaining can therefore be said to account for change in that measure of family relationship at Time 2. This is because the stability of each variable is included within the model, that is, the association between each variable at Time 1 and Time 2 (pathways  $\gamma_1$  and  $\gamma_2$  in Figure 2.6). The cross lagged model is fully saturated therefore no fit statistics are generated.



**Figure 2.6 Cross lagged panel model**

The reciprocal effects model (Figure 2.7) assesses the influence of each variable on the other within time points (pathways  $\beta_1$  and  $\beta_2$  in Figure 2.7), but also includes the stability of both variables in the model (pathways  $\gamma_1$  and  $\gamma_2$  in Figure 2.7). This model therefore determines if each variable is having an impact on the other simultaneously. The reciprocal effects model has 1 degree of freedom and therefore the fit of the model can be assessed. A number of indices were used to give an overall impression of goodness of fit:  $\chi^2$  with 1 degree of freedom, the goodness of fit index (GFI) and the adjusted goodness of fit index (AGFI). As with the twin models, a non-significant  $\chi^2$  statistic suggests that the model is not significantly different to the data and therefore suggests a good fit. The GFI and AGFI statistics range from 0 to 1, with a value of 1 representing a good fit to the data. The difference between the GFI and the AGFI also indicates how well the model fits (Kelloway, 1998).



**Figure 2.7 Reciprocal effects model**



Cross lagged panel analysis is advantageous over conducting a number of regression analyses because the coefficients are simultaneously estimated and therefore problems with multiple testing are avoided. Another advantage of using cross lagged panel analysis is that because both variables are measured at both time points it is possible to examine change in the variables and the effects of each on the other (as discussed in the previous paragraphs). However, there are also some limitations to the use of cross lagged panel analysis. If the measures being used are not reliable the coefficients in the models may in fact be artifactual. That is, if one of the measures is not particularly reliable, the stability coefficient will be low and this will therefore provide the other variable with more scope to explain the variance (because little has been explained by the stability of the variable). Similarly if there is a great deal of stability in a variable, there will be very little scope for the other variable to show any influence because so much of the variance is already explained by the stability of the initial variable. These limiting factors therefore need to be considered when examining the results of cross lagged panel analyses.

#### *Testing whether a pathway differs for different groups*

Stacked models were also used in order to test for differences between groups. One pathway (e.g.  $\gamma_3$ ) can be equated across two models (identical models with different participants, e.g. a cross lagged model for males and a cross lagged model for females). The change in model fit from the initial model to the one with the paths equated across models is then examined. Where the  $\chi^2$  statistic is significant, this suggests that the pathway cannot be equated across groups as there is a significant change in model fit, therefore the pathway is significantly different for the two groups.

## **Chapter Summary**

This chapter has detailed the samples, procedures and measures used in both the CaStANET and the SWFS. These two studies will be utilised in the next chapters to address the aims of this thesis. I have also outlined the methodology of the analyses which will be used in the following chapters. Specific details pertaining to each chapter will be described within method sections of the respective chapters.

## **Chapter 3. Genetic Influences on ADHD Symptoms and their Continuation**

### **Introduction**

This chapter examines the genetic aetiology of ADHD symptoms using the CaStANET sample. Possible differences for males and females in the proportion of variance explained by genetic and environmental factors are examined. The contribution of genetic and environmental factors to the continuation of ADHD symptoms is also examined in a longitudinal sub-sample of CaStANET.

### *Genetic Influences on ADHD Symptoms*

ADHD has been shown to be highly heritable with heritability estimates in the region of 60 to 88% (Rutter, 2006). A number of twin studies contribute to the evidence that genetic factors account for a large proportion of the variation in ADHD symptoms (e.g. Gjone, Stevenson & Sundet, 1996; Goodman & Stevenson, 1989; Haberstick et al., 2008; Hudziak et al., 2005; Martin et al., 2002; Nadder et al., 1998; Polderman et al., 2007; Rietveld et al., 2004; Thapar et al., 2000). Both additive genetic and non-additive genetic influences have been shown along with non-shared environmental influences, whereas shared environmental influences tend to be small or non-significant. For example, previous studies using the CaStANET sample when the twins were younger have shown additive genetic, non-additive genetic and unique environmental factors to influence children's ADHD symptoms when reported by parents (Martin et al., 2002; Thapar et al., 2000; Thapar, Harrington & McGuffin, 2001). Studies using other twin samples have also shown additive and non-additive genetic factors and non-shared environmental factors to explain the variation in ADHD symptoms (Hudziak et al., 2005; Polderman et al., 2007; Rietveld et al.,

2004). A small number of studies have shown shared environmental influences on parent reports of ADHD (Hay, Bennett, Levy, Sergeant & Swanson, 2007; Steffensson et al., 1999).

A number of twin studies have also shown contrast effects on maternally reported ADHD symptoms (e.g. Thapar et al., 1995; Price et al., 2005; Kuntsi et al., 2005). For example, Thapar and colleagues (2000) showed that, measured on a trait level, both the Inattention subscale of the DuPaul ADHD rating scale and Rutter A scale showed significant contrast effects (but the overall DuPaul ADHD measure showed additive and non-additive genetic and non-shared environmental influences but no contrast effects). Contrast effects occur when a high score in one twin corresponds with a lower score in their cotwin. There are two possible explanations for the presence of contrast effects. Firstly this may be due to interaction between siblings, in that the behaviour of one twin is having an effect on the other. Secondly this could be due to rater bias, that is, parents are rating their twins as more dissimilar because they are comparing the behaviour of one twin with their cotwin.

Differentiating these explanations is difficult, however Simonoff et al. (1998) suggested that the explanation of rater bias is more plausible than interaction between siblings because the effects are not apparent for teacher reports of children's behaviour. Also contrast effects have been found particularly in young children and it has been suggested that the rater bias may be more evident at this younger age when parents may have fewer other children to compare their children with (Rietveld et al., 2004). Nadder et al. (2001) however suggest that the contrast effect is not just rater bias but also report bias as they showed contrast effects for interview measures.

Contrast effects result in MZ and DZ twin correlations being reduced, but this affects the DZ twins to a greater extent than MZ twins and thus the effects appear

similar to those of non-additive genetic influences (Simonoff et al., 1998). Contrast effects also have an effect on the variance of scores in that it is increased, again with this affecting DZ twins to a greater extent. The presence of contrast effects is therefore suggested if the correlation between MZ twins is greater than twice that of DZ twins and particularly where the DZ twin correlation is near to zero or negative, also if the variance of the trait in DZ twins is greater than that of MZ twins.

Whether contrast effects or non-additive genetic effects have been found, high heritability estimates have been shown for ADHD symptoms. The first aim of this chapter is to examine the genetic aetiology of ADHD symptoms within the CaStANET sample of twins in the 2004 data collection point when they were aged between 12 and 20 years old.

#### *Genetic Influences on the Continuation of ADHD: Evidence from Twin Studies*

Not only is there a wealth of evidence suggesting that genetic factors account for much of the variation in ADHD symptoms (Rutter, 2006) but strong genetic contributions have also been shown to influence the continuation of ADHD symptoms. This has been shown in a number of different twin samples at different ages. Van den Berg et al. (2006) used the Netherlands Twin Registry to examine ADHD symptoms in young adulthood (18 to 30) and found that 77% of the stability in ADHD symptoms was accounted for by genetic factors. In a sample of twins that were 8 and 9 years at baseline and followed up at age 13 and 14 years, Larsson, Larsson and Lichtenstein, (2004) showed stability in ADHD symptoms to be influenced mostly by genetic factors (between 74 and 79% of stability) and change mostly influenced by genetic influences and non-shared environmental influences. Using a further wave data collected from the same sample when they were aged 16

and 17, Larsson, Lichtenstein and Larsson (2006) also showed genetic influences to account for a large amount of the overlap in inattentive and impulsive/hyperactive symptoms and their continuation over time. Similar findings of genetic influences on the continuation of ADHD symptoms were found for children who were aged 3 years at the first time point and then followed up at age 7, 10 and 12 years (Rietveld et al., 2004). Price et al. (2005) used a sample of preschoolers (aged 2 years at baseline and then followed up at age 3 and 4 years) to assess continuity in ADHD symptoms and found genetic influences account for the majority (91%) of the stability in ADHD symptoms. Further analyses of this sample, including follow up data when the twins were aged 7 and then aged 8 years, showed that between 59 and 98% of stability (correlations between .27 and .58 depending on the comparison between which age group) was accounted for by genetic factors (Kuntsi et al., 2005). In the latter two referenced studies contrast effects were found (Price et al., 2005; Kuntsi et al., 2005).

Together, these longitudinal twin studies provide strong evidence that genetic factors play an important role in the continuation of ADHD symptoms across a number of samples and different age groups. Table 3.1 shows a summary of the stability correlations for each of the longitudinal twin studies. While correlations across time points vary (the stability correlations ranged from 0.27 to 0.75) a large amount of this covariation is explained by genetic factors. The analyses in this chapter set out to replicate these findings and extend them by using a sample of twins ranging from childhood at Time 1 (5 to 13 years of age) to adolescence and young adulthood at Time 2 (12 to 20 years of age). The study therefore included children across a wide age range and one that has not been covered previously, i.e. including those in childhood and early adolescence to those in adolescence to young adulthood.

**Table 3.1 Summary of stability correlation coefficients for ADHD over time and gender difference findings from longitudinal twin studies of ADHD**

<b>Study</b>	<b>Age of twins</b>	<b>Stability correlations (<i>r</i>)</b>	<b>Gender differences</b>
Price et al., 2005	2 to 4 years	.46 to .60	No
Kuntsi et al., 2005	2 to 8 years	.27 to .58	No
Rietveld et al., 2004	7 to 12 years	.65 to .75	Yes
Larsson et al., 2004	8 to 14 years	.51	Yes
Larsson et al., 2006	8 to 14 years	.34 to .60	Yes
van den Berg et al., 2006	18 to 30 years	.42 to .58	No

*Gender Differences in the Estimates of Variance Components*

*Cross sectional studies*

Gender differences are evident for the prevalence of ADHD, with more males being diagnosed than females (Taylor et al., 1998). This gender difference is reduced in community samples (Gaub & Carlson, 1997), but mean ADHD symptoms still tend to be higher for males than females. A number of cross sectional twin studies have examined whether there are gender differences in the magnitude of genetic and environmental influences on ADHD symptoms, most of which do not find significant gender differences (e.g., Thapar et al., 1995; Simonoff et al., 1998, Hudziak et al., 2005). Importantly, the sample from which the longitudinal sub-sample in the present study was taken showed no evidence of gender differences (Thapar et al., 2000). Rhee, Waldman, Hay and Levy (1999) however, found gender differences in the magnitude of genetic and environmental influences with a model including additive genetic, shared and non-shared environmental factors fitting best for females, but a model with additive genetic, non-additive genetic and non-shared environmental

factors for males. Rietveld et al., (2003) found no gender differences in attention problem scores (CBCL; Achenbach, 1991) at ages 3 and 7, whereas at age 10 and 12 there were differences in variance between males and females (Rietveld, Hudziak, Bartels, van Beijsterveldt, Boomsma, 2003). The proportion of genetic and environmental influences is reported to be similar for males and females.

Steffensson and colleagues (1999) using the Swedish Twin Register sample found gender differences in the magnitude of genetic and environmental influences with higher heritability estimates for females, whereas males showed greater shared environmental influences in a sample of 8 and 9 years olds. At a later time point using those in the same sample (aged 13 and 14 years), males showed greater heritability than at Time 1 and shared environmental influences were not significant for either males or females (Larsson et al., 2004). While the same model (ACE) fit the data and the same pattern of results were observed for males and females, the estimates could not be constrained to be equal across gender.

### *Longitudinal studies*

Studies which are longitudinal have also examined whether there are gender differences in the variance components of ADHD. Table 3.1 shows a summary of the results of gender difference findings for longitudinal twin studies of ADHD which will now be discussed. The longitudinal analyses of the Swedish Twin Register sample were conducted separately for males and females because gender differences had been shown in both of the cross sectional analyses (Larsson et al., 2004). In terms of continuation, estimates for males and females appeared reasonably consistent with the majority of stability being attributed to additive genetic influences, similarly most of the change in ADHD scores was influenced by additive genetic influences, but



non-shared environmental influences also played a significant role. When examining gender differences in the continuation of ADHD subtypes (inattention and hyperactivity/impulsivity) Larsson et al. (2006) found that the magnitude of genetic and environmental influences was different for males and females, but the best fitting model was the same for both males and females models. Hence the authors suggest that the gender differences may be small.

In the longitudinal analyses using the Netherlands Twin Register sample, estimates for each variance component were allowed to vary by gender (Rietveld et al., 2004). Between the ages of 7 and 12 years, additive genetic influences accounted for more of the covariation across time for females than for males (Rietveld et al., 2004). Whereas for males, non-additive genetic influences had more impact upon the covariation than they did for females (Rietveld et al., 2004).

The longitudinal twin studies of ADHD which included younger twins (Price et al., 2005 and Kuntsi et al., 2005) between the ages 2 years and 8 years found gender differences only in mean and/or variance not in the magnitude of genetic and environmental influences. Similarly, in a study of twins in later adolescence and young adulthood there were no reports of gender differences in variance components (but this was not explicitly tested), but there were mean differences (van den Berg et al., 2006). These studies of young children and older adolescents therefore suggest no gender differences, but the evidence from twin studies of middle to late childhood is less clear. Gender differences were therefore examined in the CaStANET sample which included children, adolescents and young adults.

### *The Present Chapter*

This chapter aims to examine genetic and environmental influences on the continuation of ADHD symptoms and whether these influences vary for males and females. Given the previous findings, it was hypothesised that a) there would be strong genetic influences on ADHD at each time point b) there would be a moderate amount of stability in ADHD symptoms across time c) there would be evidence of genetic influences on the stability of ADHD symptoms d) differences in the magnitude of genetic and environmental influences on the continuation of ADHD symptoms for males and females were likely to be small.

### **Methods**

#### *Sample*

The univariate analyses were based on information from 1068 twin pairs where parents had completed questionnaires in the 2004 data collection point of the CaStANET (Time 2 as detailed in the General Methods Chapter). There were 15 families who had been excluded as they had no twin zygosity information (hence there were 1083 in the original sample). Overall there were 420 MZ twin pairs (195 male pairs and 225 female pairs) and 648 DZ twin pairs (147 male pairs, 169 female pairs and 332 opposite sex (OS) pairs). Twin ages ranged from 12 to 20 years with a mean of 16.09 ( $SD = 1.95$ ).

The longitudinal analysis was based on data collected at two time points approximately 8 years apart from the Greater Manchester sub-sample of CaStANET (in 1996 and 2004, from here on denoted as Time 1 and Time 2 respectively). The final longitudinal sample (i.e., those families taking part at both time points) comprised 736 twin pairs, which included 285 MZ twin pairs (137 male pairs and 148

female pairs) and 451 DZ twin pairs (95 male pairs, 128 female pairs and 228 OS twin pairs). This excluded 17 with no zygosity information and 79 where the parent did not respond at Time 2 (only the twin replied) and one ID mismatch. At Time 1 twins were aged from 5 to 15 years old ( $M = 9.15$ ,  $SD = 1.90$ ) whereas at Time 2 they were aged from 12 to 20 years old ( $M = 16.20$ ,  $SD = 1.90$ ).

### *Procedure*

At both time points, questionnaires were sent to parents of twins on the CaStANET register (as described in the General Methods Chapter). Within the main sample (Time 2) 94% (1000/1068) of parent questionnaires were completed by the mother. Of those in the longitudinal sub-sample, 93% of parent questionnaires were completed by the mother at the earlier (Time 1) data collection point.

### *Measures*

ADHD symptoms were measured using the modified DuPaul scale (1991) as detailed in the General Methods Chapter.

### *Analysis*

Data analysis was carried out using the twin modelling package Mx (Neale et al., 1999). Having examined the MZ and DZ twin correlations, univariate genetic models were then fitted to the data as outlined in the General Methods Chapter. As a preliminary to the longitudinal analyses, univariate analyses were carried out at each time point using only the longitudinal sub-sample to confirm similar results to the full sample. Next, a bivariate cholesky decomposition was fit to the data. This allowed Time 1 and Time 2 data to be aggregated in one model and the covariation between

time points to be decomposed into genetic and environmental influences. Gender differences were also examined within this longitudinal analysis.

## **Results**

### *Descriptives of the Whole Sample (Time 2)*

For the whole sample with parent replies at Time 2 ( $n = 1068$ ), ADHD scores ranged across the complete scale of 0 to 54 with a mean of 11.66 ( $SE = .27$ ). Males scored significantly higher than females (males  $M = 13.68$ ,  $SE = .42$ , compared with females  $M = 9.84$ ,  $SE = .33$ ,  $t_{(1053)} = 7.35$ ,  $p < .001$ ). The scores were positively skewed and therefore the transformation  $\text{Ln}(\text{ADHD} + 1)$  was used so that the distribution was approximately normal. The order of the twins was randomised using the random selection function in SPSS (SPSS 12.0.2, 2004). That is, 50% of the twin pairs were selected using the random function and the order of these was switched (e.g. from twin 1 to twin 2).

### *Univariate Genetic Analyses of the Whole Sample (Time 2)*

The zygosity groups were then split by gender and correlations were calculated (Table 3.2). The pattern of correlations was similar for males and females and the DZOS twin correlation was only slightly lower than the same sex DZ twins, thus gender differences were not expected. The pattern of correlations suggested additive and non-additive genetic effects as the DZ twin correlation was slightly less than half that of the MZ twins (MZ  $r = .65$ , DZ  $r = .26$ ). Therefore an ADE model was initially fitted to the data. Previous to this however, a saturated model was fitted to the data, followed by a series of tests for zygosity and birth order effects on mean and variance, sex and age effects on ADHD scores, along with assessment of sex

effects on the variances and covariances (Table 3.3). Results showed that age and sex were both significant covariates and were thus included as covariates in further models. There were however no significant effects of birth order or zygosity on the mean or variance. Variances and covariances were also found to be equal across sexes. As there was no significant difference in MZ and DZ twin variances a contrast effects model was not suggested.

**Table 3.2 Twin correlations of ADHD scores split by zygosity and gender**

	<i>r</i>	<i>n</i>
<b>MZ males</b>	.65	185
<b>DZ males</b>	.29	132
<b>MZ females</b>	.63	209
<b>DZ females</b>	.33	159
<b>DZ same sex</b>	.33	291
<b>DZOS</b>	.27	316

A series of models to test gender differences were carried out as detailed in the analyses section of the General Methods Chapter. The ‘no gender effects’ model was found to be an acceptable representation of the data as the parameter estimates could be constrained to be equal for males and females without a significant drop in model fit (Table 3.4). Overall, a model which showed additive genetic and non-shared environmental influences which were of the same magnitude for males and females was chosen as the most acceptable model because the non-additive genetic parameter was not significant ( $D = .25$ , 95% CI 0, .56) and could be removed from the model without a significant drop in model fit (Table 3.4). Additive genetic factors accounted for 64% (95% CI .58, .69) of the variation in ADHD symptoms and non-shared environmental factors accounted for the remaining 36% (95% CI .31, .42).

**Table 3.3 Saturated model and tests of differences in means, variances and covariances and testing for covariates (age and sex)**

<b>Model</b>	<b>-2LL</b>	<b>df</b>	<b><math>\Delta-2LL</math> <math>= \chi^2</math></b>	<b><math>\Delta df</math></b>	<b><i>p</i></b>	<b>AIC</b>
0. Saturated	5544.43	2029				
<b>Testing assumptions</b>						
1. Birth order effect on the mean	5545.04	2032	0.62	3	.893	-5.39
2. Zygoty effect on the mean	5545.56	2034	1.13	5	.951	-8.87
3. Birth order effect on the variance	5549.52	2035	5.09	6	.532	-6.91
4. Zygoty effect on the variance	5553.54	2037	9.11	8	.333	-6.89
5. Equality of variances across genders	5547.85	2035	3.42	6	.755	-8.58
6. Equality of covariances across gender	5544.95	2033	0.53	4	.971	-7.48
7. Significant sex effect	5596.95	2030	52.52	1	.000	50.52
8. Significant age effect	5595.94	2030	51.51	1	.000	49.51

**Table 3.4 Genetic model fitting results for ADHD symptoms including age and sex as covariates**

Model	-2LL	df	$\Delta-2LL$ = $\chi^2$	$\Delta df$	<i>p</i>	AIC	Comparison model	$\Delta\chi^2$ (df)	<i>p</i>
0.Saturated	5544.43	2029							
<b>A. Testing for gender effects</b>									
1. ADE <sub>(males)</sub> ADE <sub>(females)</sub> qualitative gender differences (A)	5556.62	2045	12.19	16	.731	-19.81			
2. ADE <sub>(males)</sub> ADE <sub>(females)</sub> qualitative gender differences (D)	5556.62	2045	12.19	16	.731	-19.81			
3. ADE <sub>(males)</sub> ADE <sub>(females)</sub> common genetic effects	5556.62	2046	12.19	17	.788	-21.81	1	0 (1)	ns
4. No gender effects ADE	5558.09	2049	13.66	20	.847	-26.34	1	1.47 (4)	.832
<b>B. Testing nested models</b>									
4. No gender effects ADE	5558.09	2049	13.66	20	.847	-26.34			
<b>5. AE</b>	<b>5560.97</b>	<b>2050</b>	<b>16.54</b>	<b>21</b>	<b>.739</b>	<b>-25.46</b>	<b>4</b>	<b>2.88 (1)</b>	<b>ns</b>

### *Univariate Analysis of the Twin Sub-Sample Data used in the Longitudinal Analyses*

Next, the longitudinal sub-sample was used to examine the effects of genetic and environmental influences on the continuation of ADHD symptoms. Those in the sub-sample ( $n = 736$ ) were compared with those only participating in the whole sample ( $n = 332$ ). Gender and zygosity did not differentiate between twins who were or were not included in the longitudinal sub-sample (gender OR = .93, 95% CI .75, 1.15; zygosity OR = 1.08, 95% CI .83, 1.41). There was however an age difference, with those included in the sub-sample being older ( $M = 16.20$  years,  $SD = 1.89$ ) than those only included in the whole sample ( $M = 15.86$  years,  $SD = 2.04$ ;  $t_{(1066)} = -2.62$ ,  $p < .01$ ). Mean ADHD symptom scores were not significantly different between the two groups (sub-sample  $M = 11.67$ ,  $SE = .33$  compared with whole sample only  $M = 11.65$ ,  $SE = .48$ ,  $t_{(1053)} = .03$ ,  $p = .97$ ).

Mean ADHD scores at Time 1 (twin mean age = 9.15 years, range 5 – 15 years) and Time 2 (twin mean age = 16.20, range 12 – 20 years) were 11.86 ( $SE = .33$ ) and 11.66 ( $SE = .33$ ) respectively. These therefore show only a very slight (and non significant,  $t_{(726)} = .67$ ,  $p = .51$ ) decrease in symptoms from Time 1 to Time 2. Males' scores were significantly higher than females both at Time 1 (males  $M = 14.54$ ,  $SE = .51$ , compared with females  $M = 9.62$ ,  $SE = .37$ ,  $t_{(735)} = 8.04$ ,  $p < .01$ ) and Time 2 (males  $M = 13.92$ ,  $SE = .53$ , compared with females  $M = 9.68$ ,  $SE = .38$ ,  $t_{(726)} = 6.56$ ,  $p < .01$ ). Age and gender had a significant impact on ADHD scores and so both were entered as covariates to each of the models fitted to the data.

Because a sub-sample was being used for the longitudinal analyses, univariate models were fitted to the smaller sub-sample to confirm whether or not the genetic architecture of ADHD symptoms in the sub-sample was the same as in the whole sample. At Time 1, the pattern of twin correlations suggested additive and non-



additive genetic influences were present as the MZ twin correlation ( $r = .71, n = 284$ ) was more than twice the correlation between DZ twins ( $r = .28, n = 448$ ). Similarly, at Time 2 additive and non-additive genetic influences were suggested by the pattern of twin correlations (MZ  $r = .66, n = 266$ , DZ  $r = .23, n = 426$ ). Models which included both these types of genetic influence were therefore fitted to the Time 1 data then to the Time 2 data. There were no significant variance differences between MZ and DZ twins at Time 1 (MZ twin 1 variance = .81, MZ twin 2 variance = .83, DZ twin 1 variance = .99, DZ twin 2 variance = .97;  $\Delta\chi^2$  comparing model with equal variances with saturated model = 4.17, 3 df,  $p = .24$ ) or Time 2 (MZ twin 1 variance = .97, MZ twin 2 variance = .94, DZ twin 1 variance = .95, DZ twin 2 variance = 1.04;  $\Delta\chi^2$  comparing model with equal variances with saturated model = 1.28, 3 df,  $p = .73$ ). The presence of contrast effects was therefore not tested within the longitudinal sub-sample.

Univariate model fitting showed that at both time points the ADE model showed an adequate fit to the data (Table 3.5). The AE model at each time point also showed an adequate fit to the data (compared with the saturated model), but at both time points the AE model showed a significant reduction in fit compared to the ADE model. Therefore within this longitudinal sub-sample the ADE model for both time points was accepted as the best representation of the data. At Time 1 additive genetic factors accounted for 33% (95% CI .00, .64) of the variance in ADHD symptoms and non-additive genetic factors accounted for 41% (95% CI .09, .75), thus an overall broad heritability estimate of 74% was found at Time 1. Non-shared environmental factors accounted for the remaining 26% of the variance in ADHD symptoms at Time 1. At Time 2, additive genetic factors accounted for 25% (95% CI .00, .61) and non-additive genetic factors accounted for 40% (95% CI .04, .70) of the variation in

ADHD symptoms. Overall heritability at Time 2 in the longitudinal sub-sample was therefore 65%. The remaining variation in ADHD symptoms at Time 2 was accounted for by non-shared environmental factors (35%, 95% CI .29, .41). Broad heritability was therefore similar in the longitudinal sub-sample and the whole sample however, there were significant non-additive genetic effects in the longitudinal sub-sample which were not present in the whole sample.

**Table 3.5 Model fitting results for univariate analyses of the longitudinal sub-sample**

Model	-2LL	df	$\Delta-2LL$ $= \chi^2$	$\Delta df$	$p$	AIC	Comparison model	$\Delta\chi^2$ (df)	$p$
<b>Time 1 1996</b>									
0. saturated	3802.53	1456							
<b>1. ADE</b>	<b>3807.15</b>	<b>1462</b>	<b>4.62</b>	<b>6</b>	<b>.593</b>	<b>-7.38</b>			
2. AE	3813.62	1463	11.09	7	.135	-2.91	1	6.47 (1)	.011
3. E	4044.84	1464	242.31	8	< .001	226.31	1	237.69 (2)	.000
<b>Time 2 2004</b>									
0. saturated	3829.41	1407							
<b>1. ADE</b>	<b>3832.05</b>	<b>1413</b>	<b>2.64</b>	<b>6</b>	<b>.853</b>	<b>-9.37</b>			
2. AE	3836.75	1414	7.34	7	.395	-6.66	1	4.70 (1)	.03
3. E	3997.65	1415	168.24	8	< .001	152.24	1	165.60 (2)	.000

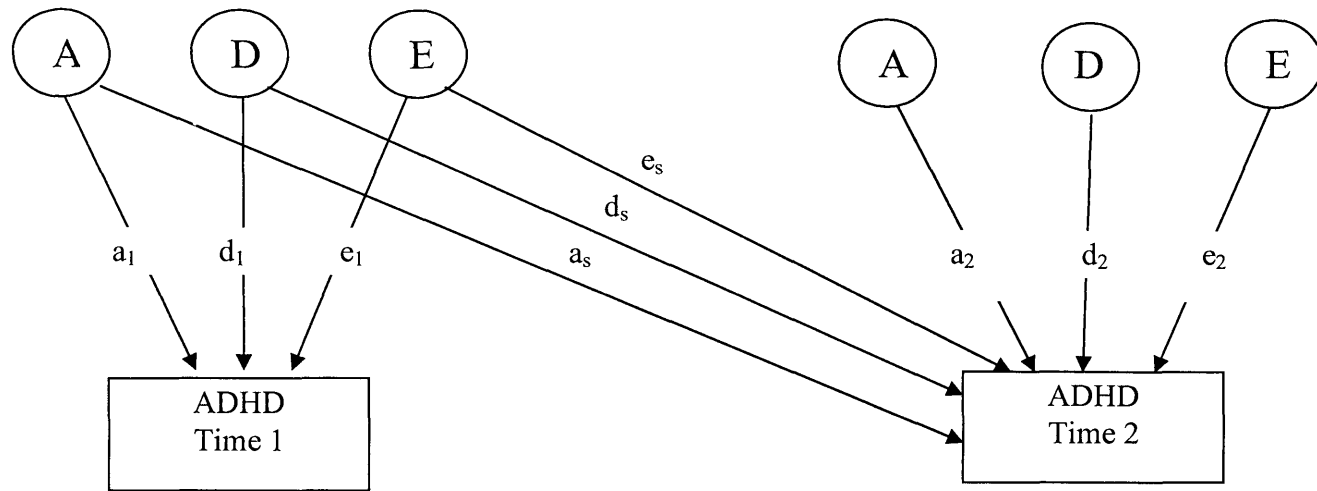
Footnote: Gender differences were not explored in these univariate analyses as these were examined in the longitudinal analyses.

### *Longitudinal Sub-Sample Analysis*

Correlations over time suggested a moderate amount of stability in ADHD symptoms (twin 1  $r = .57$ , twin 2  $r = .56$ ). Cross-twin cross-time correlations suggested significant genetic influences on the relationship between ADHD symptoms at Time 1 and Time 2 as the correlations were greater for MZ twins ( $r = .42$  and  $r = .36$ ) than for DZ twins ( $r = .17$  and  $r = .10$ ). The cross-twin cross-time correlations split by gender also suggested that there were significant genetic influences on the relationship between Time 1 and Time 2 ADHD symptoms (Table 3.6). A bivariate model which estimated additive and non-additive genetic influences as well as non-shared environmental influences was fitted to the longitudinal data. To confirm that there were no gender differences, the magnitude of genetic and environmental influences were allowed to vary by child gender. The fit of the model that included gender differences compared with the fit of the model that constrained the estimates to be equal across genders showed no significant drop in fit, hence confirming that there were no significant gender differences (Table 3.7). Subsequently, to simplify the fitting of nested models, a full bivariate model which equated parameters for males and females at the beginning and used only the two zygosity groups (i.e. MZ and DZ, rather than splitting the groups further by gender) was used. From the full bivariate model (Figure 3.1), pathways that were non-significant were systematically dropped from the model and the fit of each of the models was compared (Table 3.7). Both the additive genetic component shared between Time 1 to Time 2 (path  $a_s$  in Figure 3.1) and the non-additive genetic variance component specific to Time 2 (path  $d_2$  in Figure 3.1) could be dropped from the model without a significant drop in model fit shown by the  $\chi^2$  statistic (model 6, Table 3.7). In an alternative model both additive and non-additive genetic influences

specific to Time 2 (path  $a_2$  and  $d_2$  in Figure 3.1) could be dropped from the model without a significant drop in model fit (model 7, Table 3.7). As these two models (model 6 and 7 in Table 3.7) were not nested, the AIC was used to compare them. This showed that model 6 (Figure 3.2) with no shared additive genetic influences ( $a_s$ ) and no non-additive genetic influences ( $d_2$ ) specific to Time 2 was a more acceptable model as it had a lower AIC.

The accepted bivariate model (model 6, Table 3.7, Figure 3.2) showed that genetic factors accounted for a large amount of the stability in ADHD symptoms over time. Figure 3.2 shows the unstandardised estimates with 95% confidence intervals. These estimates can be used to calculate the amount of stability and change in ADHD scores that was due to genetic and environmental factors (Larsson et al., 2004). Stability in scores was estimated to be  $r = .52$  ( $[\.55 \times .00] + [\.63 \times .65] + [\.49 \times .23]$ ), which suggests 27% of the variance in scores at Time 2 could be explained by scores at Time 1. The majority (78%) of stability in ADHD symptoms was due to non-additive genetic influences ( $[\.63 \times .65] / .52$ ) with the non-shared environmental influences accounting for the other 22% of the stability. Additive genetic influences did not account for any of the stability in ADHD symptoms. The proportion of change due to additive genetic influences was 48%, and due to non-shared environmental influences was 52%. None of the change in ADHD symptoms was due to non-additive genetic influences.



**Figure 3.1 Bivariate longitudinal genetic model.** A = additive genetic variance component, D = non-additive genetic variance component, E = non-shared environmental variance component, a = additive genetic path, d = non-additive genetic path, e = non-shared environmental path, subscript 1 = time one, subscript s = shared across both time points, subscript 2 = time two.

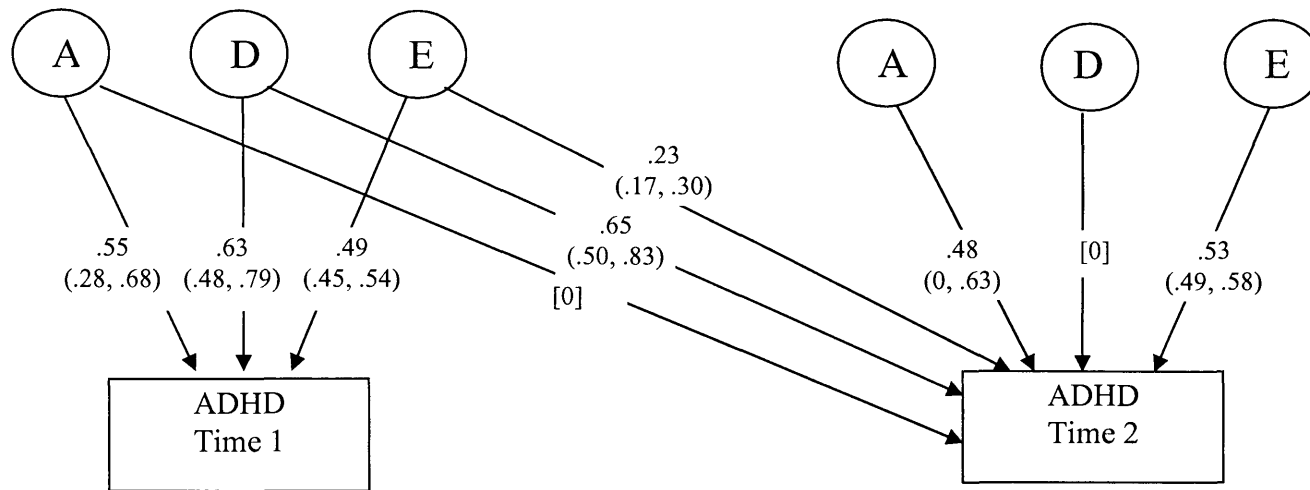
**Table 3.6 Cross-twin cross-time correlations for ADHD symptoms at Time 1 and Time 2. Results shown by gender**

		MZ twins	DZ twins same sex	DZ OS
ADHD symptoms at Time 1 and Time 2	Males	.38**	-.03	.15*
	Females	.45**	.27**	

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

**Table 3.7 Longitudinal analysis of ADHD symptoms**

Model	-2LL	df	$\Delta$ -2LL = $\chi^2$	df	$p$	AIC	Comparison model	$\Delta\chi^2$	$p$
0. Saturated model	7115.20	2811							
<b>A. Testing for gender differences</b>									
1. Gender effects Time 1 & Time 2 ADE	7172.74	2863	57.54	52	.278	-46.46			
2. No gender effects ADE	7179.51	2872	64.31	61	.362	-57.70	1	6.77 (9)	.661
<b>B. Testing nested models</b>									
0b. Saturated bivariate	7168.46	2855							
2. No gender effects ADE	7179.51	2872	11.04	17	.854	-22.96			
3. No A cross pathway	7179.51	2873	11.04	18	.893	-24.96	2	0.00 (1)	.996
4. No D cross pathway	7189.49	2873	21.03	18	.278	-14.97	2	9.99 (1)	.002
5. No E cross pathway	7189.12	2873	20.65	18	< .001	-15.35	2	53.61 (1)	< .001
<b>6. No A cross pathway or D at Time 2</b>	<b>7179.51</b>	<b>2874</b>	<b>11.04</b>	<b>19</b>	<b>.992</b>	<b>-26.96</b>	<b>2</b>	<b>0.00 (2)</b>	<b>1.000</b>
7. No A or D at Time 2	7182.82	2874	14.36	19	.762	-23.64	2	3.32 (2)	.190



**Figure 3.2 Accepted bivariate model of ADHD symptoms over time. Unsquared, unstandardised parameter estimates are shown for ease of seeing how the stability and continuity correlations are computed. A = additive genetic variance component, D = non-additive genetic variance component, E = non-shared environmental variance component.**

Footnote: Standardised parameter estimates are as follows:  $a_1 = 32\%$ ,  $d_1 = 42\%$ ,  $e_1 = 26\%$ ,  $a_s = 0$ ,  $d_s = 43\%$ ,  $e_s = 5\%$ ,  $a_2 = 23\%$ ,  $d_2 = 0$ ,  $e_2 = 29\%$ .



## Discussion

The aim of this chapter was primarily to assess the genetic aetiology of ADHD symptoms, the stability of ADHD symptoms over eight years and the contribution of genetic influences on stability. Secondly, the presence of gender specific effects was examined. The univariate analyses of ADHD symptoms in the whole of the 2004 sample showed heritability to be high with no gender differences present. As detailed in the results section, the non-additive genetic parameter in the ADE model was non-significant and there was no evidence of contrast effects as the variances for MZ and DZ twins did not differ. So when taking into account these different factors along with the fit statistics of the models, the model which included additive genetic and non-shared environmental (AE) effects was chosen as the best fitting model.

For the longitudinal analysis, a sub-sample was used. The results suggested that as expected ADHD symptoms were highly heritable at both time points. However in contrast to the whole sample in 2004, within the longitudinal sub-sample both additive genetic and non-additive genetic influences contributed to the variation in ADHD symptoms at Time 1 (1996) and Time 2 (2004). Again similar to the whole sample results, MZ and DZ twin variances at each time point did not differ and suggested that rater contrast effects were not present within the sub-sample. The stability of ADHD symptoms ( $r = .52$ ) was reasonably high and was comparable with previous twin studies (range of  $r = .27$  to  $.75$ ; Kuntsi et al., 2005; Larsson et al., 2004; Larsson et al., 2006; Price et al., 2005; Rietveld et al., 2004; van den Berg et al., 2006). A large proportion of the stability was found to be the result of genetic factors (non-additive). Gender differences were not present in the longitudinal analysis.

Many previous twin studies have shown high heritability estimates for ADHD symptoms and the results presented in this chapter further support these findings. The

univariate analyses showed that additive genetic influences accounted for 64% of the variance. The rest of the variance was accounted for by non-shared environmental influences. Within the longitudinal sub-sample however, both additive and non-additive genetic influences were shown at each time point with overall heritability reaching 74% and 66%. Evidence for the impact of non-shared environmental factors was also shown. These influences could range from a number of different factors that make twins less similar to each other as well as containing measurement error. There was no evidence for shared environmental factors contributing to ADHD scores within any of the analyses. Overall the findings are consistent with other twin studies in showing strong genetic influences on ADHD symptoms in childhood, adolescence and young adulthood.

A number of twin studies have shown contrast effects on ADHD symptoms however the results presented here do not suggest contrast effects as the variance in ADHD symptoms for MZ and DZ twins did not differ significantly. This is consistent with a previous report of the univariate analyses of the Time 1 (1996) data (Thapar et al., 2000), based on the same measure, from which a sub-sample was included in the longitudinal analyses in this chapter. The previous study (Thapar et al., 2000) showed that rater contrast effects were not suggested for the total DuPaul scale measure of ADHD symptoms but they were using the Rutter A scale and hence the authors suggest that the DuPaul scale may be less susceptible to rater bias (Thapar, et al., 2000).

Within the analyses of the whole sample, significant gender differences were not found and this is supported by previous studies which have shown no gender differences in magnitude of genetic and environmental influences on ADHD symptoms for males and females (Hudziak et al., 2005; Thapar et al., 1995; Thapar et

al., 2000; Simonoff et al., 1998). It should however be noted that there were gender effects on the mean and thus gender was included as a covariate. The need to include gender as a covariate is unsurprising as mean level differences in ADHD symptoms are often found for males and females. It is interesting that no gender differences were found in the longitudinal analyses because the other two longitudinal twin studies which examined gender differences and included a similar age group to the CaStANET sample (Rietveld et al., 2004 and Larsson et al., 2004) found slightly differing results. The longitudinal study by Rietveld and colleagues (2004) found additive genetic influences to be more prominent for the continuation of girls ADHD symptoms than boys. In contrast, the results presented in this chapter showed that not only was it possible to equate parameters for males and females, but also the additive genetic pathway from Time 1 to Time 2 was non-significant suggesting no influence of additive genetic factors on ADHD stability. The study by Larsson and colleagues (2004) also varied to the present study, because parameter estimates for males and females could not be equated and because additive genetic factors were shown to have a significant impact upon the continuation of ADHD symptoms.

The 95% confidence intervals for the genetic parameter estimates were wide, with those of the additive genetic effects having a lower value of zero and thus were non-significant. Testing a model which has non-additive genetic influences but no additive genetic influences is biologically unlikely (Martin et al., 2002), hence even though the additive genetic influences were non-significant these were not removed from the model.

One explanation for the wide confidence intervals is that there is low power to detect non-additive genetic influences, as very large sample sizes are needed to detect them (Rietveld et al., 2003). However this would not explain why the confidence

intervals are wide for the additive genetic influences as well as the non-additive genetic influences within the longitudinal sub-sample univariate analyses. An alternative explanation could be that the wide range of ages accounts for the wide confidence intervals. This could be the case if the relative contribution of genetic and environmental factors on ADHD symptoms differs by age of child. Age was included as a covariate as it had a significant effect on the mean, however differences in variance proportions may still be possible. Given the different results for the relative role of genetic and environmental factors and gender effects shown by studies of ADHD using samples of different age groups (as discussed in the introduction section of this chapter), this explanation, while not tested here, seems plausible.

Overall the results in this chapter support previous twin studies in demonstrating a moderate stability in ADHD symptoms over time and that this is to a large extent influenced by genetic factors (e.g. Larsson et al., 2004; Price et al., 2005). It appears therefore that genetic factors influence not only ADHD symptoms at a particular point in time but they also influence the continuation of ADHD symptoms. Environmental factors were also shown to play a role in the continuation of symptoms, with 22% of the stability being accounted for by non-shared environmental influences. Previous longitudinal twin studies have also shown non-shared environmental factors having an impact upon continuity. For example, Larsson et al. (2004) report non-shared environmental influences on continuity to be 10% and 15% for boys and girls respectively. Other studies have shown proportions between 6 and 41% (van den Berg et al., 2006; Kuntsi et al., 2005; Price et al., 2005).

The majority of change in ADHD symptoms in the present study was accounted for by non-shared environmental factors. Larsson et al. (2004) found that a moderate amount (38 to 45%) of change was accounted for by non-shared

environmental factors, however in contrast to the present study, genetic factors accounted for most of the change in ADHD symptoms. The non-shared environmental estimate includes measurement error and this may partly account for the non-shared environmental effect on change in ADHD symptoms. There may also be a number of non-shared environment factors which are resulting in this influence on change in ADHD scores. Larsson et al. (2004) suggest that this could be due to socialisation by peers, parents and teachers. The way twins are differentially treated could have an impact upon their ADHD symptoms. This may particularly be the case for peers and teachers who may be different people for each twin in a pair. However, these factors may not only have an impact which would be observed as non-shared environmental influences, genes may also play a role. Children and adolescents may evoke particular behavioural responses from others and if their behaviour or symptoms are heritable, such is the case with ADHD symptoms, and these are evoking responses from others then evocative gene-environment correlation may be present. A number of studies are consistent with the presence of evocative rGE particularly for negative parenting (Ge, Conger et al., 1996; Neiderhiser et al., 2004; O'Connor et al., 1998). If this is the case, the effect of these genetically influenced environmental factors will be included within the genetic component explaining variance rather than the non-shared environmental.

### *Limitations*

Some limitations to the analyses included within this chapter should be noted. Firstly, the longitudinal sub-sample did not include the whole sample. Comparisons between the main sample and the sub-sample however showed no difference in ADHD symptoms, but those in the sub-sample were older.

The confidence intervals around the estimates for additive and non-additive genetic influences within the longitudinal sub-sample were wide. The reasons for this are not clear. This may be due to heterogeneity effects. There might be variation in variance components over the different ages. Not only did the sample include a wide range of ages at both time points, there was also quite a long period of time between Time 1 and Time 2.

### *Conclusions*

The results in this chapter have supported previous studies which have shown that ADHD symptoms are highly heritable and genetic influences account for a large amount of stability in ADHD symptoms. However, even though genetic factors accounted for a large amount of the continuation of ADHD symptoms environmental factors were also shown to play a significant role both in the stability and change in symptoms. Furthermore, as detailed within the discussion, where there are genetic influences on exposure to risk environments the effects of these will be included within the genetic variance component rather than non-shared environmental. Careful determining of the specific environmental factors which have an effect on ADHD symptoms and the mechanisms through which they may operate is the next step in understanding the continuation of ADHD. The next chapter will therefore examine the association between specific family relationship factors and ADHD symptoms.

## **Chapter 4. Genetic and Environmental Mediation of the Association between ADHD Symptoms and Parent-Child Warmth and Hostility**

### **Introduction**

In the previous chapter genetic factors were shown to have a significant impact upon ADHD symptoms and their continuation. However genetic factors do not account for all of the variation in symptoms, thus exploring the effects of possible environmental factors, specifically family relationships, was one of the key aims of this thesis. In this chapter the association between ADHD symptoms and warmth and hostility in the parent-child relationship is examined to ascertain whether these family relationship measures may have a causal risk effect on ADHD symptoms by testing the extent to which the association between these dimensions of the parent-child relationship and ADHD symptoms are environmentally mediated rather than only genetically mediated. This is examined using the CaStANET sample, however, the data for this sample on specific parent-child relationship dimensions is only available at one time point (Time 2). Thus, the direction of influences in these associations is assessed using the longitudinal SWFS sample.

As discussed in the main introduction, family relationship factors have been shown to have an influence on children's externalising behaviour and studies focusing specifically on ADHD have shown associations with negative family relationships (Barkley, 1998; Biederman et al., 1995a). Not only have strong genetic influences been shown on ADHD symptoms, twin studies have also shown that family relationships are influenced to some extent by genetic factors (Kendler & Baker, 2007). That there are genetic influences on environmental factors such as family relationships leads us to question the nature of the relationship between ADHD

symptoms and family relationships. These family relationships may have true environmental influences on ADHD symptoms; however the relationship may also be genetically mediated, that is the association between the two may be due to shared genetic liability (the same genes influencing the symptoms and the relationship). Also, factors such as family relationships, which are commonly understood as risk environments, may indeed be consequences rather than antecedents to psychopathology and therefore not represent a risk factor. Thus, when examining the relationship between environmental 'risk' variables and child psychopathology it is important that to assess the direction of influence in order to determine whether they are true environmental risk factors.

#### *Genetic Influences on ADHD Symptoms*

There is a great deal of evidence from both twin and molecular genetic studies that show genetic influences on ADHD (Thapar, Langley, Owen & O'Donovan, 2007). Strong genetic contributions have also been shown to influence the continuation of the disorder when measured at a trait level (e.g., Larsson, Larsson & Lichtenstein, 2004). These findings have also been supported by the results in the previous chapter that showed genetic influences both on ADHD symptoms in adolescence/young adulthood as well as on the continuation of symptoms over time from childhood through to adolescence and young adulthood. While there is therefore much evidence for the genetic contribution to ADHD symptoms, previous studies as well as the findings within this thesis also show that environmental factors play a role in the aetiology and continuation of ADHD. This highlights the importance of examining more closely which specific environmental factors may have an influence on ADHD symptoms.



### *Genetic Influences on Family Relationships and the Possibility of Genetic Mediation*

A number of genetically informative studies examining different aspects of the parent-child relationship have shown that children's genes have an impact upon family relationships (Kendler & Baker, 2007). Therefore, where family relationships and children's symptoms or behaviours are both influenced by genetic factors, there is the possibility that the genetic influence is a confounding variable. That is, the apparent association between the child's outcome and the family relationship may be spurious because the same genetic factors influence both. This is known as a genetically mediated relationship. Genetically informative samples provide a solution to examining the relationship between two variables as shared genetic influences can be taken into account and therefore an assessment of an environmentally mediated relationship can be considered. The hypothesis that the relationship between the variable of interest is due to shared genetic influences can be tested against an alternative that there is a true environmental effect using a genetically sensitive design (Rutter, 2005). Previous studies have shown that after controlling for genetic influences, there is evidence of environmentally mediated effects between the parent-child relationship and child psychopathology, for example the effect of maltreatment on antisocial behaviour (Jaffee et al., 2004). However, there is little research which has examined this relationship for ADHD symptoms specifically.

### *Are Family Relationships a True Environmental Risk Factor for ADHD Symptoms?*

Not only do genetic factors need to be taken into consideration when assessing whether a risk factor has a potential causal effect on an outcome, but also the effect of the risk factor needs to be established. That is, an assumed risk factor and an outcome

may be associated, but the direction of this association needs to be from the risk factor to the outcome variable if any conclusions about its causal effect are to be drawn.

Longitudinal study designs can therefore be used to establish the direction of a relationship and is therefore another key feature suggested by Rutter (2005) needed to assess true environmental effects.

There is an increasing recognition of bidirectional influences between parents' behaviour and that of their children as discussed in the Introduction Chapter.

Therefore, rather than family relationships having an impact on children's ADHD symptoms, there is evidence which suggests that children's ADHD symptoms may have an influence on the parent-child relationship. For example, Schachar et al. (1987) found that medication given to children with ADHD and or conduct disorder which improved their behaviour, also improved the mother-child relationship in that there were more displays of warmth and fewer negative exchanges.

As previously mentioned, the results from the Multimodal Treatment Study of Children with ADHD (MTA) do not show a clear cut relationship between improvement in ADHD symptoms and in parent-child relationships. Medication and combined treatment (medication with behaviour therapy) both improved ADHD symptoms during the trial to a greater extent than the community comparison group (MTA Cooperative Group, 1999). If there were a direct and reasonably immediate effect of ADHD symptoms on parent-child relationship, these two groups would be expected to show the most change in parent-child relationship. However, it was the combined treatment and behaviour therapy only groups which showed significantly greater improvement in parent-child relationship than community care comparison group (MTA Cooperative Group, 1999). Specifically examining negative parenting behaviour, improvements were found in all three treatment groups compared with the

community care comparison (Wells et al., 2000). Positive parenting on the other hand was not shown to differ across the groups (Wells et al., 2000). Observational measures of parent-child relationship showed a greater improvement in constructive parenting for the combined treatment compared with medication or community comparison (Wells et al., 2006). These results suggest that there is not a uniform, direct and immediate impact of improvement in ADHD symptoms on parent-child relationship. However, it must be noted that each of these groups were receiving treatment of some kind; many in the community care group were on medication and thus it is a comparison of different treatments and the magnitude of their effects rather than comparing with a control group. The behaviour therapy would be partly be focusing on the interactions between parent and child and thus changes in this relationship would be expected as part of the treatment not necessarily related to a reduction in ADHD symptoms.

Many different characteristics of the parent-child relationship have been described and examined with regard to their effect on children's adjustment. These include negative aspects of parenting behaviour, conflict and rejection, each of which has been referred to here in relation to children's behavioural problems. Other specific dimensions of the parent-child relationship such as high levels of hostility and low warmth have also been found to have a detrimental effect on children's behaviour (Paley, Conger & Harold, 2000). Caspi and colleagues (2004) found an effect of mother-child warmth on children's anti-social behaviour. Similarly, Ge, Best and colleagues (1996) showed effects of parent-child hostility on children's conduct disorder (both reported by mother and by father) as well as warmth on conduct problems (reported by father). Indeed they also showed an association between both

mother and father warmth and hostility associated with presence of adjustment problem (either conduct or depressive symptoms).

In a longitudinal genetically informative community sample, Burt, McGue, Krueger & Iacono (2005) examined the relationship over 3 years between parent-child conflict and a composite of externalising behaviours, comprising of CD and ODD symptoms. Not only did they show bidirectional effects (externalising behaviour having an influence on parent-child conflict and vice versa) but at each time point, shared environmental influences accounted for most of the association between externalising behaviour and parent-child conflict with genetic influences accounting for a smaller proportion (Burt et al., 2005). In a previous cross-sectional study using the same sample, Burt, Krueger, McGue and Iacono (2003) considered a latent externalising factor that also included ADHD symptoms (as well as conduct and ODD symptoms) and found evidence for both genetic and environmental mediation of the association with parent-child conflict. Both genetic and environmental pathways from parent-child conflict to this broader externalising factor were significant, thus suggesting both genetic and environmental mediation (Burt et al., 2003). Shelton et al. (2008) have recently shown that there is evidence of both environmental and genetic mediation of the relationship between mother-child warmth and hostility and conduct problems. Thus these studies suggest that there is both genetic and environmental mediation of the association between aspects of the parent-child relationship and children's conduct and oppositional behaviours (Burt et al., 2003; Burt et al., 2005; Shelton et al., 2008). The extent to which the findings will be similar when examining ADHD symptoms rather than conduct problems will be examined in the current study. Also, the relationship between ADHD symptoms and father-child warmth and hostility will be explored. There is less research that has focused on the father-child

relationship and this may differ to the mother-child relationship and therefore warrants more investigation.

### *The Present Chapter*

In this chapter parent-child warmth and hostility were examined in relation to ADHD symptoms both in the genetically informative sample (CaStANET) and the longitudinal community sample (SWFS). The extent to which the relationship between ADHD symptoms and each family relationship factors was genetically and environmentally mediated was explored within the genetically informative study. It was hypothesised that there would be both genetic and environmental mediation. Next, the relationship between ADHD symptoms and each family relationship factor was examined within and across time in the longitudinal sample. It was hypothesised that bidirectional relationships would exist between ADHD symptoms and family relationships.

## **Methods**

### *Samples*

Both the CaStANET and the SWFS were used for the analyses in this chapter. While descriptions of both are found in the General Methods Chapter, the sub-samples that were selected for analyses are described in this chapter.

#### *CaStANET*

A sub-sample of 943 twin-pairs aged between 11 and 17 years of age ( $M = 15.3$ ,  $SD = 1.4$ ) from the CaStANET (Time 2, 2004 data collection) were included in this chapter. Twins who were aged 18 and over were not included so that the sample

included adolescents rather than adolescents and young adults. Parent-child relationships may vary with age, this may be particularly so when children reach adulthood. Legally in the UK adulthood is classed as when children turn 18, they are therefore able to make their own choices. Children over the age of 18 are also less likely to be living at home as they are likely to be in employment or at university. It was therefore decided to use only those up to age 18 within this sample. Twins who were not living with their parents or each other were also excluded from the analyses (25 pairs) and those with no zygosity information were also excluded (18 pairs). Three pairs were also removed as there was ambiguity about which child the parent was reporting on.

### *SWFS*

The second sample included families from the first two waves of data collection of the SWFS. Children were therefore aged between 11–14 years ( $M = 11.68$  yrs at Time 1,  $SD = 0.47$ ,  $n = 152$  males and 157 females).

### *Measures*

#### *ADHD symptoms*

Children's ADHD symptoms were measured in the CaStANET sample using the modified DuPaul scale (DuPaul, 1991; Thapar et al., 2000) as described in the General Methods Chapter. In the SWFS the Attention Problems subscale of the CBCL (Achenbach, 1991) was used to measure children's ADHD symptoms. Mothers' reports on the attention problem scale were used through out these analyses so that it was the most comparable to the twin sample which asked mothers to report on their

children's ADHD symptoms. As described in the General Methods Chapter, internal consistency for both ADHD measures was good.

#### *Parent-child warmth & hostility*

In both samples parent-child warmth and hostility were measured using the IYFP Warmth/Hostility measure (Melby, et al. 1993). As described in the General Methods Chapter, children completed the questions twice, once with reference to their mother and once with reference to their father. Internal consistency was good for both parent-child warmth and hostility (range  $\alpha = .80$  to  $.93$ , see General Methods Chapter).

#### *Analyses*

##### *Univariate genetic analyses*

Initial correlational analyses of the CaStANET data were used to guide the model fitting. Univariate twin modelling was then carried out using Mx (Neale, Boker, Xie & Maes, 1999), as described in the General Methods Chapter, for ADHD symptoms (to check the model was the same for those under 18 years old and living at home) and for each family relationship variable. Where significant effects of twin order or zygosity on means or variances were found within the models that tested assumptions after the saturated model, these are reported in the results section. Non-significant findings are not reported. Where covariates were non-significant the saturated model was estimated again so that the comparison model is correct.

*Bivariate twin analyses: genetic and environmental mediation*

The correlation between ADHD symptoms and each of the family relationship variables was established. The survey commands in Stata 9.0 (StataCorp, 2005) were used in order to control for the non-independence of twin data. The survey commands recognise that each twin pair forms a cluster and this is taken into account in the analyses. Where there was a moderate and significant association between family variable and ADHD symptoms, bivariate genetic analyses were undertaken. Cross-twin cross-trait correlations were calculated for each zygosity as an initial assessment of a genetically mediated relationship. If the DZ cross-twin cross-trait correlation is half or less than half the magnitude of the MZ twin cross-twin cross-trait, this is suggestive of a genetically mediated relationship. However, if the DZ twin cross-twin cross-trait correlation is more than half that of the MZ twins, environmental mediation is suggested. A bivariate correlated factors twin model was then fitted to the raw data for ADHD symptoms and each of the family relationship variables. This model not only decomposes the variance of each variable into genetic and environmental influences but also estimates the association between these latent factors by decomposing the covariation of the two traits. A second method used to test for environmental mediation includes only MZ twins. This has also already been described in the General Methods Chapter. Difference scores for ADHD symptoms and each family relationship variable were computed for MZ twins (difference score = twin 1 score – twin 2 score) and then correlated. A positive correlation suggests environmental mediation.



### *Longitudinal analyses*

Cross lagged panel correlation and reciprocal effects analyses were used to assess the directional nature of the relationship between ADHD symptoms and parent-child relationship where significant correlations were found. A cross lagged model was first used to assess the relationship across time and a reciprocal effects model was then employed to assess the direction of influences within time whilst controlling for the stability in each variable. These models were fit to the data using the statistical package LISREL (LISREL 8.80; Jöreskog & Sörbom, 2006) as described in the General Methods Chapter. Where variation in the pattern of results was shown between child genders, stacked modelling was used to assess whether these were significantly different from each other.

## **Results**

### *CaStANET Preliminary Analyses*

In the genetically informative twin sample the mean ADHD score was 12.5 ( $SE = .31$ ). Males tended to score higher than females (male  $M = 14.91$ ,  $SE = .37$ ; female  $M = 10.23$ ,  $SE = .49$ ,  $t_{(794)} = 7.85$ ,  $p < .01$ ). Mean scores for mother-child warmth and hostility were 26.20 ( $SE = .22$ ) and 14.31 ( $SE = .21$ ) respectively. For the father-child relationship, the mean score for warmth was 24.48 ( $SE = .27$ ) and for hostility was 14.71 ( $SE = .24$ ). Mean mother-child warmth was significantly greater than father-child warmth ( $t_{(604)} = 9.81$ ,  $p < .01$ ), whereas mean father-child hostility was significantly greater than mother-child hostility ( $t_{(605)} = 2.01$ ,  $p < .05$ ). There were no child gender differences in reports of mother- or father-child warmth or hostility (range  $t = .09$  to 1.32, all *ns*).

ADHD symptom scores were transformed with the transformation Ln (ADHD+1) so that they approximated a normal distribution. Mother and father-child warmth scores were also skewed, hence an inverse square root (SQRT[36-warmth]) transformation was applied. For warmth therefore, a high score reflected low warmth because the inverse transformation had been applied. Transformed scores were used in all of the following analyses.

Age was significantly correlated with mother-child warmth ( $r = .11, p < .001, n = 1536$  individuals) and hostility ( $r = .09, p = .003, n = 1542$  individuals) as well as father-child warmth ( $r = .13, p < .001, n = 1174$  individuals). The correlation between father-child hostility and age however did not quite reach statistical significance ( $r = .07, p = .07, n = 1161$  individuals). Therefore, quality of parent child relationship appeared to deteriorate with age. Age was included as a covariate (and tested for its significance) within the analyses of parent-child relationship and ADHD symptoms.

ADHD symptoms and mother-child hostility were moderately correlated ( $r = .27, p < .01, n = 1365$ ). When splitting the sample by child gender, moderate correlations were found for mother-child hostility and ADHD symptoms both for males ( $r = .31, p < .01, n = 633$ ) and females ( $r = .25, p < .01, n = 732$ ). The correlation between ADHD symptoms and warmth however was low ( $r = .09, p < .01, n = 1356$ ). For females the correlation reached significance ( $r = .12, p < .01, n = 727$ ), but for males the correlation remained low and non-significant ( $r = .07, p = .13, n = 629$ ). A similar pattern of correlations emerged for the father-child relationship variables. There was a moderate correlation between ADHD symptoms and father-child hostility ( $r = .26, p < .01, n = 1030$ ), which when split by child gender also showed moderate significant correlations (males  $r = .31, p < .01, n = 478$ ; females  $r = .22, p < .01, n = 552$ ). There was a weak correlation between ADHD symptoms and

father-child warmth ( $r = .09, p = .01, n = 1039$ ) which, similar to the mother-child warmth correlations, reached statistical significance for females ( $r = .11, p = .02, n = 559$ ) but did not for males ( $r = .07, p = .22, n = 480$ ).

### *Univariate Genetic Analyses*

Twin correlations for ADHD symptoms and each of the family relationship variables are shown in Table 4.1. These correlations were used to guide the model fitting. In the case of ADHD symptoms these analyses were also informed by the results of Chapter 3 which showed an AE model without gender differences to be the model which represented the data well. The analyses of ADHD symptoms in this chapter were conducted as a preliminary to the bivariate model fitting to confirm that the same model accepted for the whole sample in Chapter 3 also fit this sub-sample (of twins aged under 18 years) adequately.

#### *ADHD symptoms*

The correlation between ADHD scores for MZ twins was greater than twice that of DZ twins (MZ  $r = .62$ , DZ  $r = .26, p < .01, n = 760$  pairs) suggesting the presence of non-additive genetic effects. Age and gender were both significant covariates and thus were included in each model to account for these effects. Gender differences were not expected given the results of Chapter 3 and the pattern of twin correlations across the 5 zygosity groups (MZ males  $r = .58$ , DZ males  $r = .20$ , MZ females  $r = .65$ , DZ females  $r = .38$ , DZOS  $r = .31$ ) however gender models were fit to the data to formally examine gender differences. Variances did not significantly differ based on zygosity (fit for model which constrained variances by zygosity within

twin order and gender  $\chi^2_{(8)} = 10.82, p = .212, AIC = -5.18$ ) and therefore a rater contrast effects model was not tested.

**Table 4.1 Twin correlations for each family variable and ADHD symptoms in reduced sub-sample split by gender and zygosity**

		Split by gender and zygosity					
		Males		Females		Opposite sex	Same sex
<i>n</i>		MZ	DZ	MZ	DZ	DZ	DZ
ADHD symptoms	760	.58	.20	.65	.38	.31	.32
Mother-child hostility	722	.66	.41	.59	.13	.20	.25
Father-child hostility	538	.71	.40	.65	.36	.26	.38
Mother-child warmth	716	.61	.59	.62	.47	.27	.50
Father-child warmth	554	.60	.54	.66	.46	.33	.52

**Table 4.2 Model fit results for ADHD symptoms (age and gender included as covariates)**

Model	-2LL	df	$\Delta-2LL$ = $\chi^2$	$\Delta df$	<i>p</i>	AIC	Comparison model	$\Delta\chi^2$ (df) comparison	<i>p</i>
0. Saturated	4157.07	1529							
<b>A. Testing for gender effects</b>									
1. ADE <sub>(males)</sub> ADE <sub>(females)</sub> qualitative gender differences (A)	4170.93	1545	13.86	16	.609	-18.14			
2. ADE <sub>(males)</sub> ADE <sub>(females)</sub> common genetic (A) effects	4170.93	1546	13.86	17	.677	-20.14	1	0 (1)	ns
3. No gender effects (ADE)	4173.84	1549	16.77	20	.668	-23.23	1	2.91 (4)	.573
<b>B Testing nested models</b>									
3. No gender effects (ADE)	4173.84	1549	16.77	20	.668	-23.23			
<b>4. AE</b>	<b>4174.62</b>	<b>1550</b>	<b>17.55</b>	<b>21</b>	<b>.677</b>	<b>-24.45</b>	<b>1</b>	<b>0.78 (1)</b>	<b>ns</b>

Models examining gender differences were fitted to the ADHD data (Table 4.2). While the models which estimated qualitative or quantitative gender differences all showed adequate fits to the data, a model which included no gender differences was also an adequate fit ( $\Delta\chi^2_{(20)} = 13.86$ ) and did not differ significantly to the models which included gender differences. Within the ADE model with no gender differences however, the parameter estimate for D was not significant (95% CI .00 to .49). The non-additive genetic influence was then dropped from the model and the resulting AE model showed a good fit to the data. The AE model was not significantly different to the ADE model and the AIC was lower. The AE model was therefore found to be the most acceptable model for the data. This model showed that additive genetic effects accounted for 63% (95% CI .56 to .69) of the variation in ADHD symptoms, and non-shared environmental factors accounted for the remaining 37% (95% CI .31 to .44) of the variation. Thus the genetic architecture for this sub-sample is the same as for the full sample described in Chapter 3.

#### *Mother-child hostility*

The pattern of twin correlations for mother-child hostility suggested that different factors may be influencing the variation in mother-child hostility for boys compared with girls (Table 4.1). The DZ male correlation was more than half that of the MZ male correlation, thus suggesting shared environmental factors may be present. For girls however, the correlation between DZ twins was less than half that of the MZ twins and therefore non-additive genetic influences may be present. The correlations for DZ OS twins and same sex DZ twins were quite similar and therefore qualitative gender differences were not expected. It is of note that variances were found to differ depending on birth order (fit for model which constrained variances for

twin 1 and twin 2 within zygoty  $\chi^2_{(6)} = 16.93, p = .010, AIC = 4.93$ ) but means did not (fit for model which constrained means within zygoty  $\chi^2_{(3)} = .34, p = .953, AIC = -5.66$ ).

A full ACE model for males and ADE model for females was then fitted to the data (Table 4.3). Qualitative gender differences were not found within this model (model 2 not different to model 1). To test for overall quantitative gender differences, a model which estimated ACE to be equal for males and females was fitted (model 3, Table 4.3) followed by a model which estimated ADE to be equal for males and females (model 4, Table 4.3). Neither of these models showed an adequate fit to the data as the  $\chi^2$  showed a significant drop in model fit compared with the saturated model. It was concluded therefore that there were gender differences.

As gender differences were found, the model with ACE for males and ADE for females ( $ACE_{(males)} ADE_{(females)}$ ) was then used as the full model from which parameters were dropped and model fit was compared. Firstly, D for females was dropped from the full model and then C for males, followed by a model which dropped both (i.e. included only AE and for males and females). The  $AE_{(males)} ADE_{(females)}$  and the  $ACE_{(males)} AE_{(females)}$  both showed an adequate fit to the data (non-significant  $\chi^2$ ) whereas the  $AE_{(males)} AE_{(females)}$  model was a poor fit to the data. Neither  $AE_{(males)} ADE_{(females)}$  nor  $ACE_{(males)} AE_{(females)}$  showed a significant drop in fit compared with the  $ACE_{(males)} ADE_{(females)}$  model. As these two models were not nested within each other, the AIC values were used to decide which model was the more acceptable model. The  $AE_{(males)} ADE_{(females)}$  model showed the lowest AIC value and was therefore selected as the most acceptable model. For males, additive genetic factors accounted for 68% (95% CI .59, .75) of the variance in mother-child hostility and the remaining 32% (95% CI .25, .41) of the variance was accounted for



by non-shared environmental factors. For females, additive genetic factors accounted for 17% (95% CI .02, .44) of the variance in mother-child hostility, non-additive genetic factors accounted for a further 39% (95% CI .10, .57) of the variance and the remaining 44% (95% CI .36, .55) was accounted for by non-shared environmental factors.

### *Father-child hostility*

The pattern of correlations for father-child hostility suggested shared environmental influences may be present along with additive genetic and non-shared environmental factors because the correlation for DZ twins was greater than half that of the MZ twin correlation for both males and females (Table 4.1). Therefore an ACE model was fitted to the data. Models testing for qualitative and quantitative gender differences were fitted to the data (Table 4.4). While each of the models showed an adequate fit to the data, the model which did not include gender differences was found to be the most acceptable as it is more parsimonious (i.e. uses the least number of parameters) and did not differ to the model which included gender differences based on  $\Delta\chi^2$ . The shared environmental factor was then removed from the model. The resulting model fit the data well and did not show a significant drop in fit to the ACE model. The AE model with no gender differences was therefore accepted as the best representation of the data. Additive genetic factors accounted for 66% (95% CI .59, .72) of the variation in father-child hostility and non-shared environmental factors accounted for 34% (95% CI .28, .41) of the variance.

**Table 4.3 Model fitting results for mother-child hostility (age included as a covariate)**

Model	-2LL	df	$\Delta-2LL = \chi^2$	$\Delta df$	<i>p</i>	AIC	Comparison model	$\Delta\chi^2$ (df) comparison	<i>p</i>
0. Saturated	9883.09	1517							
<b>A. Testing for gender effects</b>									
1. ACE <sub>(males)</sub> ADE <sub>(females)</sub> qualitative gender differences (A)	9908.45	1533	25.37	16	.064	-6.63			
2. ACE <sub>(males)</sub> ADE <sub>(females)</sub> common effects (A) on males and females	9908.45	1534	25.37	17	.087	-8.63	1	0 (1)	ns
3. No gender effects ADE	9921.05	1537	37.97	20	.009	-2.03			
4. No gender effects ACE	9924.50	1537	41.41	20	.003	1.41			
<b>B. Testing nested models</b>									
2. ACE <sub>(males)</sub> , ADE <sub>(females)</sub> common (A) effects on males and females	9908.45	1534	25.37	17	.087	-8.63			
5. ACE <sub>(males)</sub> AE <sub>(females)</sub>	9911.48	1535	28.40	18	.056	-7.61	2	3.03 (1)	ns
<b>6. AE<sub>(males)</sub> ADE<sub>(females)</sub></b>	<b>9909.18</b>	<b>1535</b>	<b>26.09</b>	<b>18</b>	<b>.098</b>	<b>-9.91</b>	<b>2</b>	<b>0.72 (1)</b>	<b>ns</b>
7. AE <sub>(males)</sub> AE <sub>(females)</sub>	9915.74	1536	32.65	19	.026	-5.35			

**Table 4.4 Model fitting results for father-child hostility (age included as a covariate)**

<b>Model</b>	<b>-2LL</b>	<b>df</b>	$\Delta-2LL = \chi^2$	$\Delta df$	<i>p</i>	<b>AIC</b>	<b>Comparison model</b>	$\Delta\chi^2$ (df) comparison	<i>p</i>
0. Saturated	7549.65	1136							
<b>A. Testing for gender effects</b>									
1. ACE <sub>(males)</sub> ACE <sub>(females)</sub> qualitative gender differences (A)	7563.79	1152	14.14	16	.588	-17.86			
2. ACE <sub>(males)</sub> ACE <sub>(females)</sub> common genetic effects	7564.18	1153	14.53	17	.629	-19.47	1	0.39 (1)	ns
3. No gender effects ACE	7567.14	1156	17.49	20	.621	-22.51	1	3.35 (4)	ns
<b>B. Testing nested models</b>									
3. No gender effects ACE	7567.14	1156	17.49	20	.621	-22.51			
<b>4. AE</b>	<b>7567.14</b>	<b>1157</b>	<b>17.49</b>	<b>21</b>	<b>.681</b>	<b>-24.51</b>	<b>3</b>	<b>0 (1)</b>	<b>ns</b>

### *Mother-child warmth*

The twin correlations for mother-child warmth suggested that shared environmental factors might be present (Table 4.1). The twin correlations for male MZ and male same sex DZ twins were very similar (MZ males  $r = .61$  and DZ males  $r = .59$ ) and therefore suggested that there may not be genetic influences on male reports of mother-child warmth. For females however the MZ correlation was greater than the DZ correlation suggesting genetic influences. The comparison of the same sex DZ twin correlation with the DZ OS twin correlation suggested that there may be qualitative gender differences (i.e. different genes having an impact upon mother-child warmth for males than for females) as these correlations were quite different ( $r = .50$  vs.  $r = .27$  respectively). Also, the covariances could be constrained to be equal across genders, but this model was approaching significance (covariances equal across sexes within zygosity  $\Delta\chi^2_{(4)} = 9.45, p = .051, AIC = 1.45$ ). ACE models which tested for gender differences were therefore fitted to the data.

There was no evidence of qualitative gender differences as the correlation between DZ OS twins could be constrained to .5 without a significant drop in model fit (Table 4.5). The model with no gender differences was not a good fit to the data as the  $\chi^2$  statistic showed that it was significantly different to the saturated model. The model with no gender differences also showed a significantly worse fit to the data than the model which allowed estimates to vary by gender. Therefore it was concluded that there were quantitative gender differences for mother-child warmth.

A nested model which dropped the additive genetic factor for males was fitted to the data and compared with the full model of ACE for males and ACE for females. This model was a good fit to the data and did not show a significant drop in fit compared to the full model. The CE<sub>(males)</sub> ACE<sub>(females)</sub> model was therefore accepted

as a good representation of the data. For males, shared environmental factors accounted for 59% (95% CI .50, .67) of the variation in mother-child warmth scores and non-shared environmental factors accounted for 41% (95% CI .33, .50) of the variance. For females, additive genetic factors accounted for 47% (95% CI .32, .60) of the variance, shared environmental factors accounted for 15% (95% CI .05, .27) of the variance and non-shared environmental factors accounted for the remaining 38% (95% CI .31, .48) of the variation in mother-child warmth scores.

#### *Father-child warmth*

The pattern of twin correlations for father-child warmth suggested shared environmental influences for both males and females (Table 4.1). The MZ and DZ correlations for male twin pairs were more similar to each other than those for females twin pairs, thus suggesting a smaller amount of additive genetic influences for males than females. Also, similar to mother-child warmth, the comparison of same sex DZ correlations with DZ OS twins suggested that there may be some qualitative genetic gender differences. Gender differences were therefore examined with an ACE model. Each of the models which included qualitative, quantitative or no gender differences provided adequate fits to the data (Table 4.6). The ACE model with no gender effects did not show a significant drop in fit compared to the full gender differences model and was therefore taken as a better fit as it was more parsimonious. Thus, no gender differences were found.

The additive genetic factor was then dropped from the ACE model followed by a model which dropped the shared environmental factor. The AE model showed a good fit to the data where as the CE did not show a good fit to the data. When comparing the AE with the ACE, there was no significant reduction in fit using the

$\Delta\chi^2$  statistic. Thus overall the AE model was selected as the most acceptable model for the data. In this model additive genetic factors accounted for 64% (95% CI .57, .70) of the variation in children's perceptions of warmth in the father-child relationship and non-shared environmental factors accounted for 36% (95% CI .30, .43) of the variance.

**Table 4.5 Model fitting results for mother-child warmth (age included as a covariate)**

Model	-2LL	df	$\Delta-2LL$ = $\chi^2$	$\Delta df$	<i>p</i>	AIC	Comparison model	$\Delta\chi^2$ (df) comparison	<i>p</i>
0. Saturated	4698.78	1511							
<b>A. Testing for gender effects</b>									
1. ACE <sub>(males)</sub> ACE <sub>(females)</sub> qualitative gender differences (A)	4712.49	1527	13.72	16	.621	-18.28			
2. ACE <sub>(males)</sub> ACE <sub>(females)</sub> common genetic effects	4713.83	1528	15.05	17	.592	-18.95	1	1.33 (1)	.248
3. No gender effects ACE	9744.96	1531	46.18	20	.001	6.18	1	32.46 (4)	.000
<b>B. Testing nested models</b>									
2. ACE <sub>(males)</sub> ACE <sub>(females)</sub> common genetic effects	4713.83	1528	15.05	17	.592	-18.95			
4. CE <sub>(males)</sub> ACE <sub>(females)</sub>	4713.83	1529	15.05	18	.658	-20.95	2	0 (1)	ns

**Table 4.6 Model fitting results for father-child warmth (age included as a covariate)**

Model	-2LL	df	$\Delta-2LL$ = $\chi^2$	$\Delta df$	<i>p</i>	AIC	Comparison model	$\Delta\chi^2$ (df) comparison	<i>p</i>
0. Saturated	3628.77	1149							
<b>A. Testing for gender effects</b>									
1. ACE <sub>(males)</sub> ACE <sub>(females)</sub> qualitative gender differences (A)	3645.48	1165	16.71	16	.404	-15.29			
2. ACE <sub>(males)</sub> ACE <sub>(females)</sub> common genetic effects	3645.89	1166	17.13	17	.446	-16.87	1	0.41 (1)	.520
3. No gender effects ACE	3651.31	1169	22.55	20	.312	-17.45	1	5.83 (4)	.212
<b>B. Testing nested models</b>									
3. No gender effects ACE	3651.31	1169	22.55	20	.312	-17.45			
<b>4. AE</b>	<b>3654.52</b>	<b>1170</b>	<b>25.76</b>	<b>21</b>	<b>.216</b>	<b>-16.24</b>	<b>3</b>	<b>3.21 (1)</b>	<b>ns</b>
5. CE	3666.58	1170	37.81	21	.014	-4.19	3	15.26 (1)	< .001



### *Genetic or Environmental Mediation: Bivariate variance components analysis*

As noted already, ADHD symptoms showed correlations of greater than  $r = 0.2$  with both mother-child hostility and father-child hostility. The covariation between ADHD symptoms and mother-child hostility and between ADHD symptoms and father-child hostility was decomposed into genetic and environmental factors to examine the nature of the association between each pair of variables. Warmth was not further tested because there was little association with ADHD symptoms.

#### *Mother-child hostility and ADHD symptoms*

Cross-twin cross-trait correlations suggested that there were genetic influences contributing to the association between ADHD symptoms and hostility in the mother-child relationship as the cross-twin cross-trait correlations were greater for MZ twins than DZ twins (Table 4.7). Bivariate model fitting results for ADHD symptoms and mother-child hostility are shown in Table 4.8. The pattern of cross-twin cross-trait correlations for mother-child hostility was similar for males and females. However, gender differences were found for mother-child hostility in the univariate analysis and gender differences were therefore examined within the bivariate analyses. A full gender effects ADE bivariate model (i.e. ADE for ADHD symptoms and for mother-child hostility as well as allowing for different magnitudes of each for males and females) was compared with a bivariate ADE model which constrained estimates for males and females to be equal. Results showed that there were significant gender differences as the model which constrained the parameter estimates across gender was not a good fit to the data and was a significantly worse fit than the full model (Table 4.8). Given the pattern of findings in the univariate analyses, a nested model which dropped the non-additive genetic effects on ADHD symptoms and on mother-son

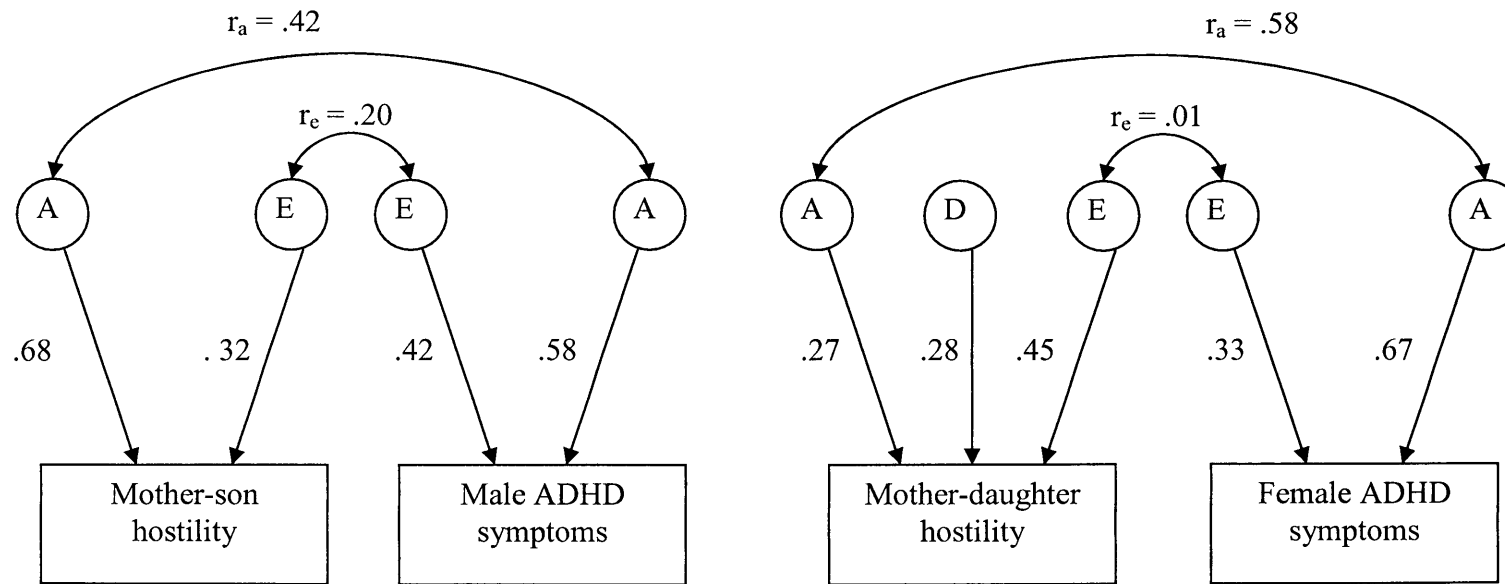
hostility ( $AE_{(\text{hostility males})}$   $AE_{(\text{ADHD males})}$ ,  $ADE_{(\text{hostility females})}$   $AE_{(\text{ADHD females})}$ ) was then fitted to the data. This provided a good fit to the data and did not show a significant reduction in model fit compared with the full gender effects ADE model. Next the non-additive genetic effects on mother-daughter hostility was also dropped from the model, but this showed a significant drop in model fit. The model which included A and E influences for males and females on ADHD symptoms, A and E influences on mother-son hostility and A, D and E influences on mother-daughter hostility was the most acceptable model (model 3, Table 4.8, Figure 4.1). The results for this model showed a genetic correlation between mother-child hostility and ADHD symptoms of  $r = .42$  (95% CI .28, .56) for males and  $r = .58$  (95% CI .38, .79) for females, thus suggesting genetic mediation for both males and females (full results of each parameter estimate are shown in Table 4.10 and Figure 4.1). For males however, there was also evidence of environmental mediation as the correlation between non-shared environmental influences on mother-son hostility and ADHD symptoms was significant ( $r = .20$ , 95% CI .03, .39).

**Table 4.7 Cross-twin cross-trait correlations for parent-hostility & ADHD symptoms. Results shown by gender**

		<b>MZ twins</b>	<b>DZ twins same sex</b>	<b>DZ twins OS</b>
ADHD & Mother- child hostility	Males	.21*	.07	.22**
	Females	.35**	.02	
ADHD & Father- child hostility	Males	.32**	.17	.20*
	Females	.29**	.11	

**Table 4.8 Bivariate model fitting results for mother-child hostility and ADHD symptoms**

<b>Model</b>	<b>-2LL</b>	<b>df</b>	$\Delta$ -2LL= $\chi^2$	<b>df</b>	<i>p</i>	<b>AIC</b>	<b>Comparison model</b>	$\Delta\chi^2$ (df)	<i>p</i>
0. Saturated	13902.100	3022							
<b>A. Testing for gender effects</b>									
1. Gender effects									
ADE (hostility males) ADE (ADHD males)	13962.69	3074	60.59	52	.194	-43.41			
ADE (hostility females) ADE (ADHD females)									
2. No gender effects	13990.81	3083	88.71	61	.012	-33.29	1	28.12 (9)	.001
ADE (hostility) ADE (ADHD)									
<b>B. Testing nested models</b>									
1. Gender effects									
ADE (hostility males) ADE (ADHD males)	13962.69	3074	60.59	52	.194	-43.41			
ADE (hostility females) ADE (ADHD females)									
<b>3. AE (hostility males) AE (ADHD males)</b>	<b>13971.50</b>	<b>3079</b>	<b>69.40</b>	<b>57</b>	<b>.126</b>	<b>-44.60</b>	<b>1</b>	<b>8.81 (5)</b>	<b>.117</b>
<b>ADE (hostility females) AE (ADHD females)</b>									
4. AE (hostility males) AE (ADHD males), AE (hostility females) AE (ADHD females)	13976.50	3080	74.40	58	.072	-41.60	1	13.81 (6)	.032



**Figure 4.1 Bivariate genetic analyses results of the relationship between mother-child hostility and ADHD symptoms**

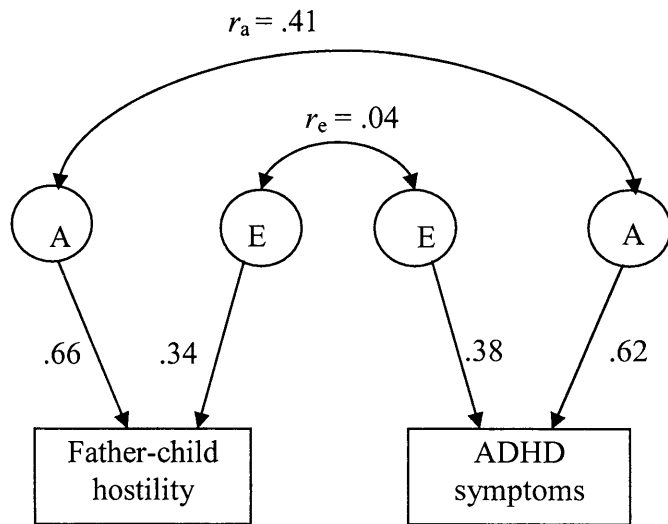
### *Father-child hostility and ADHD symptoms*

Cross-twin cross-trait correlations for father-child hostility and ADHD symptoms suggested a genetically mediated relationship for males as the MZ correlations were greater than the DZ correlations (Table 4.7). For females however, the pattern of correlations was less clear as to the relationship between ADHD symptoms and father-daughter hostility because one of the MZ cross-twin cross-trait correlations was of a similar strength to the DZ correlations. Gender differences were tested within the bivariate analyses. Because gender differences were not found within the univariate analyses for ADHD symptoms or father-child hostility gender differences were not expected. However the correlation between ADHD symptoms and father-child hostility was greater for males ( $r = .31$ ) than for females ( $r = .22$ ), thus gender differences may be present and were therefore tested.

The univariate analyses for both ADHD symptoms and father-child hostility showed AE models represented the data well, hence a bivariate AE model was used to examine the relationship between them. The results showed that there were no significant gender differences as the AE model constraining parameter estimates to be equal for males and females did not show a significant drop in model fit to the AE model which allowed for gender differences (Table 4.9). The results for the model which was the most adequate representation for the data (AE with no gender differences) are presented in Table 4.10 and shown in Figure 4.2. The relationship between father-child hostility and ADHD symptoms was genetically mediated as the correlation between additive genetic factors influencing each trait was  $r = .41$  (95% CI .30, .46). There was no evidence of environmental mediation as the correlation between non-shared environmental factors was not significant (Table 4.10).

**Table 4.9 Bivariate model fitting results for father-child hostility and ADHD symptoms**

Model	-2LL	df	$\Delta-2LL$ = $\chi^2$	df	<i>p</i>	AIC	Comparison model	$\Delta\chi^2$ (df)	<i>p</i>
0. Saturated	10593.94	2272							
<b>Testing for gender effects</b>									
1. Gender effects									
AE <sub>(hostility males)</sub> AE <sub>(ADHD males)</sub>	10663.18	2330	69.24	58	.148	-46.76			
AE <sub>(hostility females)</sub> AE <sub>(ADHD females)</sub>									
2. No gender effects									
AE <sub>(hostility)</sub> AE <sub>(ADHD)</sub>	10668.67	2336	75.03	64	.163	-52.97	1	5.79 (4)	.447



**Figure 4.2 Bivariate genetic analyses results of the relationship between father-child hostility and ADHD symptoms**



**Table 4.10 Parameter estimates for the accepted bivariate models for mother-child hostility and ADHD symptoms (A) and for father-child hostility and ADHD symptoms (B). 95% confidence intervals follow each parameter in brackets**

<b>A. Mother-child hostility and ADHD symptoms</b>	<b>Mother-child hostility</b>			<b>Correlation</b>		<b>ADHD symptoms</b>	
	A	D	E	<i>r</i> A	<i>r</i> E	A	E
Males	0.68* (.58, .75)	-	0.32* (.25, .42)	0.42* (.28, .56)	0.20* (.03, .39)	0.58* (.47, .68)	0.42* (.32, .53)
Females	0.27* (.12, .49)	0.28* (.04, .46)	0.45* (.36, .56)	0.58* (.38, .79)	0.01 (-.15, .16)	0.67* (.58, .74)	0.33* (.26, .42)
<b>B. Father-child hostility and ADHD symptoms</b>	<b>Father-child hostility</b>			<b>Correlation</b>		<b>ADHD symptoms</b>	
	A	D	E	<i>r</i> A	<i>r</i> E	A	E
Males and females	0.66* (.59, .72)	-	0.34* (.28, .41)	0.41* (.30, .46)	0.04 (-.09, .17)	0.62* (.54, .68)	0.38* (.32, .46)

### *Testing for Environmental Mediation using MZ Twin Differences*

MZ twin difference scores were also used to assess whether non-shared environmental influences were shared between ADHD symptoms and the family relationship variables and further test for environmental mediation. Age and gender were included as covariates. Because gender differences had been shown for mother-child hostility, the analysis of MZ twin differences was carried out separately for each child gender here. For males there was a significant correlation between difference in hostility scores and difference in ADHD symptom scores ( $r = .23, p = .02, n = 108$ ). In contrast, for females there was no significant correlation between difference scores ( $r = .02, ns, n = 130$ ). These results are therefore consistent with the bivariate variance components analysis suggesting evidence of environmental mediation for males but not for females for mother-child hostility.

For mother-child warmth the univariate genetic analyses suggested gender differences in the proportion of variance attributed to genetic and environmental factors, therefore the correlation between MZ difference scores was computed separately for males and females. These results showed no significant correlation between difference scores of ADHD symptoms and mother-child warmth (males  $r = -.15, ns, n = 107$ ; females  $r = -.14, ns, n = 128$ ). These correlations were of a similar magnitude for males and females, and when combined for the whole sample a correlation of similar magnitude which did reach statistical significance was obtained ( $r = -.14, p = .03, n = 235$ ). This suggests that the correlations for each gender separately were not statistically significant due to the small sample size. It may be therefore that there is some environmental mediation of the relationship between mother-child warmth and ADHD symptoms. This had not been explored using the

bivariate genetic model because the correlation between ADHD symptoms and mother-child warmth was too low to decompose into genetic and environmental factors.

ADHD difference scores and father-child hostility difference scores were not significantly correlated ( $r = .06$ , *ns*,  $n = 179$ ). These results are therefore also consistent with the bivariate variance components analysis suggesting no environmental mediation. The correlation between difference scores for father-child warmth and ADHD symptoms were also non-significant ( $r = -.04$ , *ns*,  $n = 183$ ).

### *Longitudinal Analyses*

Although evidence for environmental mediation was found for ADHD symptoms and mother-son hostility, the twin data were cross sectional. Therefore child effects on the mother cannot be ruled out. Thus, next the effects of family relationship on ADHD and vice versa were tested using the SWFS. Mean mother reports of ADHD symptoms were 3.56 ( $SD = 3.34$ ) at Time 1 and 3.42 ( $SD = 3.24$ ) at Time 2. Significant gender differences were found in that males scored higher than females at both at Time 1 (males  $M = 4.03$ ,  $SD = 3.24$ , females  $M = 3.10$ ,  $SD = 3.39$ ,  $t_{(301)} = 2.45$ ,  $p = .02$ ) and at Time 2 (males  $M = 3.83$ ,  $SD = 3.40$ , females  $M = 2.99$ ,  $SD = 3.02$ ,  $t_{(298)} = 2.27$ ,  $p = .02$ ). There were no significant gender differences in reports of mother-child relationship except for hostility at Time 1 (males  $M = 14.14$ ,  $SD = 5.46$ , females  $M = 12.84$ ,  $SD = 5.11$ ,  $t_{(294)} = 2.12$ ,  $p = .04$ ). At Time 2 the mean mother-child hostility score was 13.65 ( $SD = 5.74$ ). Mother-child warmth means were 29.63 ( $SD = 4.84$ ) and 27.90 ( $SD = 6.12$ ) at Time 1 and 2 respectively. There were no significant (child) gender differences in the father-child relationship measures. Mean father-child hostility scores were 12.87 ( $SD = 5.44$ ) and 12.78 ( $SD = 6.31$ ) at Time 1

and 2 respectively. Mean father-child warmth scores were 28.04 ( $SD = 5.94$ ) and 26.37 ( $SD = 6.65$ ) at Time 1 and 2 respectively.

ADHD scores were square root transformed as they were positively skewed, mother-child warmth scores were negatively skewed thus scores were inverse square root transformed. Mother-child hostility however was approximately normally distributed. ADHD symptoms and mother-child warmth were not significantly correlated within time or over 1 year ( $r = -.01$  to  $.07$ ,  $n = 287$ ). As there was no significant association between mother-child warmth and ADHD symptoms no further analyses were carried out.

Because child gender differences in the relationship between ADHD symptoms and mother-child hostility had been found in the genetically informative study, analysis of this relationship was examined by each gender separately in the longitudinal sample. For males both ADHD symptoms and mother-son hostility showed stability across time as the within variable, across time correlations were moderate to high (ADHD  $r = .73$ , hostility  $r = .47$ ,  $n = 140$ ). ADHD symptoms and mother-son hostility were moderately correlated both within and across time (Table 4.11). Cross lagged panel analysis showed stability across time of ADHD symptoms and mother-child hostility for males (Figure 4.3). The cross lagged pathways showed that ADHD symptoms at Time 1 had a significant influence on mother-son hostility at Time 2, but mother-son hostility at Time 1 did not significantly influence ADHD symptoms in males at Time 2. Overall, 54% of the variance in Time 2 ADHD scores and 24% of the variance of Time 2 mother-child hostility was explained by the model. A reciprocal effects model showed that ADHD symptoms also had a significant impact on mother-son hostility at Time 2 when levels of each variable at Time 1 were

controlled for. This model provided a good fit to the data,  $\chi^2_{(1)} = 0.14$ ,  $p = .71$ , GFI = 1.00, AGFI = 1.00.

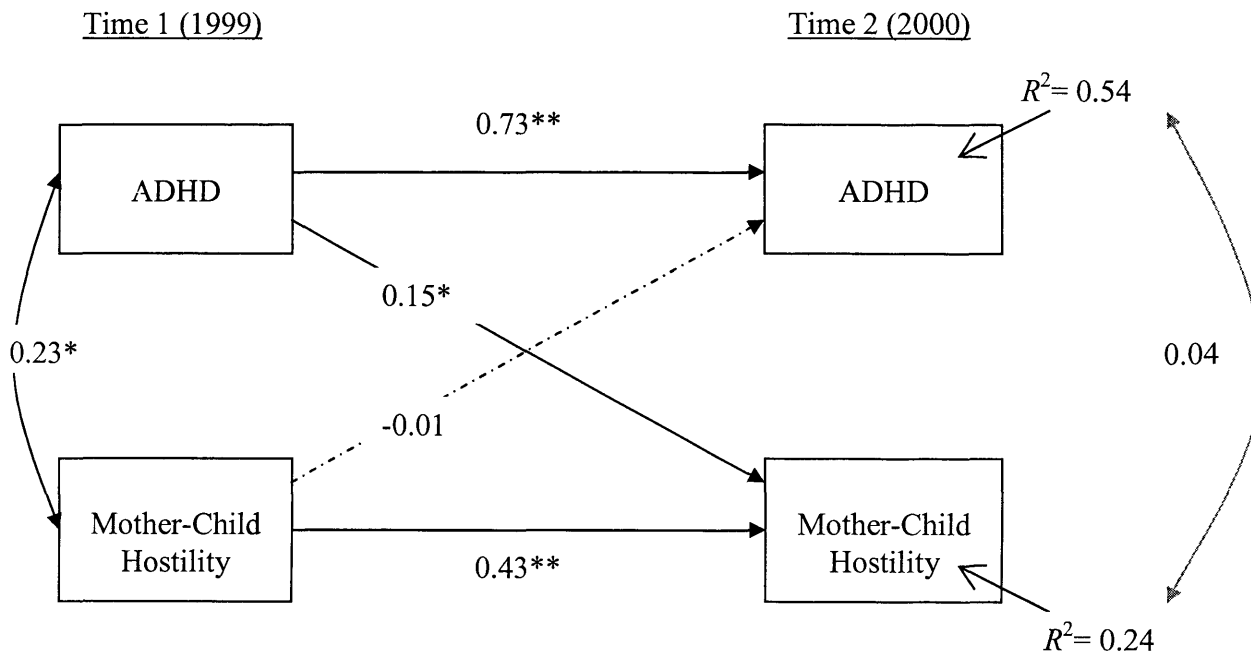
**Table 4.11 Correlations between ADHD symptoms and mother-child hostility at Time 1 and Time 2 ( $n = 140$  males and 142 females)**

		Time 1		Time 2		Mean	SD
	Males	ADHD	Hostility	ADHD	Hostility		
Time 1	ADHD	-				1.81 <sup>†</sup>	0.90
	Hostility	.23**	-			14.11 <sup>†</sup>	5.51
Time 2	ADHD	.73**	.16	-		1.69 <sup>†</sup>	0.99
	Hostility	.25**	.47**	.22**	-	13.33	5.29
<b>Females</b>							
Time 1	ADHD	-				1.41	0.89
	Hostility	.18*	-			12.68	5.04
Time 2	ADHD	.74*	.13	-		1.36	0.98
	Hostility	.13	.57*	.15	-	13.67	5.79

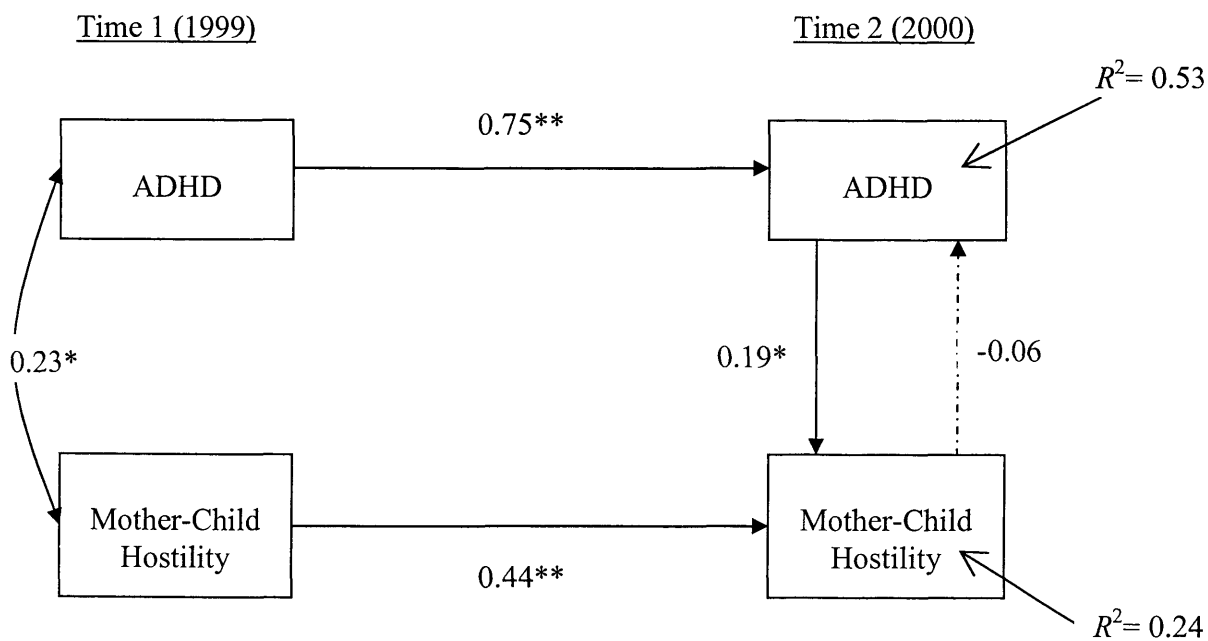
\*\*  $p < .01$ , \*  $p < .05$ , <sup>†</sup> significantly greater than for females.

**Figure 4.3 Maximum likelihood estimation of cross lagged (Panel A) and reciprocal effects (Panel B) models for ADHD symptoms of males and mother-child hostility, \* $p < .05$ , \*\* $p < .01$ .**

**Panel A**



**Panel B**



$\chi^2_{(1)} = 0.14$ , GFI = 1.00, AGFI = 1.00

For females, the correlations between ADHD symptoms across time and mother-daughter hostility across time were both significant (Table 4.11) however the only cross variable correlations which was significant was at Time 1. This pattern of correlations therefore suggests that ADHD symptoms did not have an impact on mother-daughter hostility or vice versa at Time 2. Cross lagged and reciprocal effects models were however fit to this data as a preliminary to examining differences between males and females. As expected while there was evidence of stability of each variable, none of the directional pathways between mother-daughter hostility and ADHD were significant except for the initial relationship between them at Time 1 (results not shown).

To examine whether the variation in the pattern of results for males and females was significant, a stacked modelling procedure was employed. Each of the directional pathways (each cross lagged and each reciprocal effect pathway) were in turn equated across models for males and females and change in model fit examined. The cross lagged pathway from ADHD symptoms at Time 1 to mother-child hostility at Time 2 was not significantly different for males and females ( $\Delta\chi^2_{(1)} = 1.50, ns$ ), neither was the cross lagged pathway from mother-child hostility at Time 1 to ADHD symptoms at Time 2 ( $\Delta\chi^2_{(1)} = .002, ns$ ). The reciprocal effect model pathway from ADHD symptoms at Time 2 to mother-child hostility at Time 2 did not differ for males and females ( $\Delta\chi^2_{(1)} = 1.01, ns$ ) and neither did the pathway in the opposite direction (mother child hostility to ADHD symptoms,  $\Delta\chi^2_{(1)} = 0.73, ns$ ). Therefore the stacked modelling showed that the differences between these models for males and females were not statistically significant.

The father-child relationship was next examined in the longitudinal study. Father-child hostility was square root transformed to approximate a normal distribution. There was no significant relationship between father reports of ADHD symptoms and either father-child hostility (range  $r = .07$  to  $.12$ ,  $ns$ ,  $n = 251$ ) or warmth (range  $r = -.03$  to  $.08$ ,  $ns$ ,  $n = 248$ ) both within and across time. Using mother reports of ADHD symptoms there was a weak correlation between ADHD symptoms and father-child hostility at time 1 ( $r = .13$ ,  $p < .05$ ,  $n = 275$ ) but no other correlations were significant. No further analyses were therefore conducted for father-child warmth or hostility and ADHD symptoms.

## **Discussion**

The aim of this chapter was to firstly examine whether there was an association between ADHD symptoms and a number of family relationship variables and secondly, where there was an association, to examine whether the family relationship factor had an environmentally mediated risk effect on children's ADHD symptoms. Both community samples (CaStANET and SWFS) were used. The results are initially discussed separately for each sample and then together.

Results from the genetically informative cross sectional sample (CaStANET), showed that as expected a large proportion (63%) of the variation in ADHD symptom scores was due to genetic factors. These analyses were based on a sub-sample (only those under 18 years of age and living at home) of those included within the main univariate genetic analyses (as presented in the previous chapter) and showed very similar results. The results are also consistent with a wealth of evidence from a number of other twin studies (e.g. Thapar et al., 2000; van den Berg et al., 2006). There was no evidence of shared environmental influences, but non-shared



environmental influences accounted for the remaining variation in symptoms in this sub-sample. Again these results are similar to the results for the whole sample in Chapter 3 and are consistent with previous studies.

There were significant genetic influences on children's reports of mother- and father-child hostility, father-child warmth and mother-daughter warmth. These findings are suggestive of gene-environment correlation and are supported by previous studies (Herndon, McGue, Krueger & Iacono, 2005; McGue, Elkins, Walden & Iacono, 2005; Kendler & Baker, 2007). Gender differences were found for mother-child hostility in the proportion of variance explained by genetic and environmental influences. For males additive genetic influences accounted for most of the variance in mother-son hostility (68%) with the remaining variance being explained by non-shared environmental factors. For females however 56% of the variance was explained by genetic factors, but this included both additive and non-additive genetic influences. These results are consistent with previous research in that higher heritability has been shown for males' perceptions of the parent-child relationship than females' (McGue et al., 2005). However, they differ in that greater influence of shared environmental factors were shown for females than males in the study by McGue et al. (2005), yet in the present study shared environmental factors were not found to influence mother-child hostility for males or females. Shared environmental influences were however shown to influence both mother-son and mother-daughter warmth. But, again contrary to McGue and colleagues' (2005) findings, these were more influential for males than for females. In fact more than half of the variance in mother-son warmth was accounted for by shared environmental factors and there was no evidence of genetic influence.

Significant correlations which were over a magnitude of  $r = 0.2$  were found between ADHD symptoms and both mother-child and father-child hostility. These associations were therefore explored in more detail using bivariate genetic analyses. The correlations between ADHD symptoms and mother-child and father-child warmth were of a lower magnitude and were therefore not examined using the bivariate variance components analysis. This is because the bivariate twin modelling decomposes the covariation into genetic and environmental factors, so where there is little correlation between two variables there is not a great deal of covariation to decompose and therefore the meaningfulness of the analysis is reduced.

Using two different types of bivariate analysis (bivariate genetic analysis and correlation of MZ twin differences) the relationship between ADHD symptoms and father-child hostility was found to be genetically mediated with no evidence of environmental mediation. For mother-child hostility however, results differed by child gender and an interesting pattern emerged. For females there was evidence only of genetic mediation of the association between mother-daughter hostility and ADHD symptoms. However, for hostility in the mother-son relationship there was good evidence for an environmentally mediated association as well as a genetically mediated association. Firstly, in the bivariate variance components analysis both the correlation between additive genetic influences on mother-son hostility and on ADHD symptoms and the correlation between non-shared environmental influences on these variables was moderate and significant. Thus, even when genetic mediation is accounted for there is evidence for environmental mediation of this relationship. Secondly, when examining only MZ twins, the non-shared environmental factors that affect ADHD symptoms were significantly associated those which affect mother-son hostility, again supporting an environmentally mediated process. Together both of

these analysis techniques suggest that when genetic influences are taken into account there is evidence of an environmentally mediated relationship between males' ADHD symptoms and mother-son hostility. Because the results from the twin study were cross sectional, the direction of this association could not be assessed, hence the longitudinal SWFS was used.

Results from the longitudinal sample showed that mother-son hostility was significantly influenced by boys' ADHD symptoms, thus not supporting the notion that mother-son hostility has a causal effect on ADHD symptoms. For the other parent-child relationship dimensions assessed there was no evidence of directional associations. That is, change in ADHD symptoms was not influenced by parent-child warmth or hostility, also change in mother-child warmth, father-child warmth and hostility or mother-daughter hostility were not impacted by ADHD symptoms. These findings were contrary to expectations as bidirectional influences between parent and child have been increasingly recognized and reported (Burt et al., 2005; Collins et al., 2000).

It is interesting that the pattern of results vary by child gender as well as parent gender. Hypotheses regarding the possible differences in relationship between ADHD symptoms and parent-child hostility by child gender were not initially made, but based on the gender difference results in the variance components analysis of mother-child hostility the importance of examining child gender was apparent. Previous treatment studies of children with ADHD have tended to focus on the mother-child relationship as mothers tend to be the primary caregivers and the studies also tend to focus on ADHD symptoms of boys (Barkley & Cunningham, 1979; Schachar et al., 1987) as more boys are diagnosed with ADHD (Taylor et al., 1998). The results in this chapter are consistent with these treatment studies which have shown that

effective stimulant medication for ADHD symptoms improves mother-son interactions (Barkley & Cunningham, 1979; Schachar et al., 1987). This is because when manipulated, children's (in most cases boys') ADHD symptoms are shown to have an impact on mother-child interactions, hence this is an environmentally mediated effect rather than genetic because what changes is the boys' symptoms which are influenced by the medication rather than genes. The evidence available here also provides a strong case for the environmental effect of ADHD symptoms on mother-son hostility.

The results of a significant correlation between genetic factors influencing ADHD symptoms and genetic factors influencing parent-child hostility suggest that the same genetic factors are having an impact on both. Because genetic factors do not actually have an effect on the environmental factors (such as the parent-child relationship), rather they influence behaviour which influences environmental factors (Rutter, 2006), ADHD symptoms may represent some of the child's behaviour which is the intermediate behaviour leading to mother-son hostility being genetically influenced. It is not possible however to test this in the present study. Just because two variables are influenced by genetic factors and are associated with each other does not tell us about the mechanism explaining the link (Rutter, Pickles, Murray & Eaves, 2001). What this study has shown is that after taking into account the genetically mediated relationship, there is also evidence of an environmental effect of males ADHD symptoms on mother-son hostility.

A possible reason for the differences in results for males and females could be because it is particularly the mother-son relationship which is affected by ADHD symptoms. This could be because boys show more symptoms and mothers may be more responsive to their child's behaviour than fathers. In contrast, perhaps for girls

none of them showed ADHD symptoms to a great enough extent to have an impact on mother-child hostility. This is plausible since in both samples used in this thesis females scored significantly lower than males on ADHD symptoms. Within the twin sample however the effects of gender were included as covariates so this would not have had an impact on the results, but for the longitudinal study it may be the case that some of the males' scores reached a high enough level to influence mother-child hostility, whereas females' symptom levels did not reach that point. This is just speculation and would need examining before conclusions can be drawn.

Also, a study of parents' causal attributions has also showed that parents tend to understand their sons' ADHD symptoms and behaviour as being more deliberate than their daughters and hence react more harshly (Maniadaki, Sonuga-Barke & Kakouros, 2005). However, more research is needed in this area to establish possible links between parents' causal attributions and the effect on their parenting. A more recent study which matched males and females on a number of variables (such as symptom severity and comorbidity) found no child gender differences in parents causal attributions, however parent gender differences were found (Chen, Seipp & Johnston, 2008). Fathers' positive reactions (on a continuum of pleased to upset) to inattentive and impulsive behaviours in their children showed a significant negative correlation with their attribution of causal locus of their child's behaviour (scored as a high score is more internal locus), but this association was not significant for mothers. Interestingly parents' ratings of child's control over the behaviour did not differ by child or parent gender and were not correlated with their reactions to children's behaviour. Global/stable ratings were negatively correlated with a positive reaction to children's behaviour for both mothers and fathers. However, mothers reported behaviour to be more global and stable than fathers did (Chen et al., 2008).

The findings of this chapter are important because previous research has not examined whether the association between ADHD symptoms and family relationships is environmentally mediated. Previous studies focusing on other psychopathologies have shown environmental factors to have environmentally mediated effects. For example, for conduct problems there is evidence of environmental mediation of both maltreatment and mother-child hostility (Jaffee et al. 2004; Shelton et al., 2008). Similarly, for depression, independent stressful life events have been shown to have environmentally mediated effects (Thapar, Harold & McGuffin 1998; Kendler, Karkowski & Prescott, 1999). Even though these studies are of different psychopathologies, they still guided hypotheses for this chapter in the absence of previous research specific to ADHD symptoms. The results presented here showed there was evidence for some environmental mediation for mother-son hostility and ADHD symptoms which on first inspection in the cross sectional study is consistent with research evidence on other psychopathologies and family relationships. Importantly however, when examined closer using a longitudinal design it became apparent that these findings are not consistent with previous research on other psychopathologies as the ADHD symptoms are having an environmentally mediated effect on mother-son hostility not the other way round. This highlights the importance of examining family 'risk factors' and ADHD symptoms within a longitudinal study design making it possible to assess whether the family relationship is actually a risk factor which impacts upon the continuation of the symptoms. It also highlights the importance of specifically examining ADHD symptoms as results are different to those for other psychopathologies.

### *Limitations*

Some of the differences between the two samples may be a potential limitation to this study. An ideal study design would be genetically informative as well as longitudinal. In this way the longitudinal genetic and environmental effects could be modelled. Therefore the direction *and* nature of the relationship between ADHD symptoms and parent-child hostility could be examined within one sample. The extent to which the longitudinal associations were genetically or environmentally mediated could then be established. As it is in the present study, the results suggest that the impact of mother-son hostility on ADHD symptoms is partly genetically and partly environmentally mediated, so the longitudinal pathway shown in the longitudinal sample could be showing mostly environmental mediation or mostly evocative rGE. Being able to quantify the effects of these two processes within a longitudinal framework is therefore a potential line of future research.

Because the age of the twin study crossed a broader age range (from early to late adolescence) than the longitudinal sample (early adolescence) there may be differences in the relationship between ADHD symptoms and parent-child relationships at these different stages of development. The results for the dimensions of the relationship not showing directional influences in the longitudinal sample, for example between father-child hostility and ADHD symptoms, may have varied had a different age range been examined.

A final limitation to the present study is that the extent to which the results generalise to clinical ADHD are unclear. Both samples were community based and therefore only a small proportion of children's scores would fall in the clinical range. While ADHD has been shown to act as a continuum, the results shown in these community samples need replicating in clinical samples. However, the results are

promising in suggesting that they may be generalisable firstly because they are consistent across two different community samples and secondly, because they are consistent with results from previous treatment studies of boys with a clinical diagnosis of ADHD and their interactions with their mothers.

### *Conclusions*

The present chapter set out to examine the relationship between ADHD symptoms and warmth and hostility in the both the mother- and father-child relationship using two community samples. While there was evidence of a genetically mediated relationship between ADHD symptoms and both mother- and father-child hostility, there was also evidence of environmental mediation for mother-son hostility and ADHD symptoms. This latter finding was supported using two different analytic approaches in a twin sample. The direction of this environmentally mediated effect was from boys' ADHD symptoms to mother-son hostility, thus suggesting that changes in mother-son hostility are a consequence of boys' ADHD symptoms rather than this relationship having a risk effect on ADHD symptoms. Because this relationship is environmentally mediated this offers potential for interventions to improve quality of mother-son relationship through successful management and treatment of ADHD symptoms.



## **Chapter 5. Longitudinal Associations between Family Relationship**

### **Factors and ADHD Symptoms**

#### **Introduction**

The focus of this chapter is to examine in more detail the longitudinal association between ADHD symptoms and additional family relationship factors. In the previous chapter warmth and hostility in the parent-child relationship were examined, now I will examine rejection in the parent-child relationship and conflict within the family. Firstly, rejection within both the mother-child and father-child relationship will be examined with comparisons between these in their association with ADHD symptoms also being explored. Secondly, conflict within the family will be examined as a broad measure of the family atmosphere (as described in Chapter 2) and how this is associated with ADHD symptoms.

Bidirectional effects were expected between ADHD symptoms and parent-child warmth and hostility in the previous chapter, however this hypothesis was not supported. Indeed, boys' ADHD symptoms were shown to have an effect on mother-son hostility but no other directional effects were found. The pattern of results varied depending on the dimension of parent-child relationship (warmth and hostility) and both parent and child gender. The differences in association for mother-child hostility based on child gender were directly compared, in this chapter the focus is on directly comparing the pattern of association based on the parent gender.

The two family relationship factors included in this chapter were not examined in the previous chapter. Parent-child rejection was not included in the twin study and therefore could not be examined and family conflict was reported once for both twins

in a family and therefore the genetic and environmental contributions could not be examined.

### *Parent-Child Relationships and ADHD Symptoms*

As discussed in previous chapters a number of studies including children with ADHD and their families have shown that stimulant medication which successfully reduces ADHD symptoms also improves parent-child relationships. The MTA trial (MTA Cooperative Group, 1999; Jensen et al., 2007) has looked at a number of family relationship variables including both parent report and observation measures (Hinshaw et al., 2000; Wells et al., 2000; Wells et al., 2006). However a straightforward relationship between changes in ADHD symptoms and in parent-child relationships was not shown. A study by Schachar et al. (1987) found that improvements in ADHD symptoms from stimulant medication co-occurred with more warmth and less criticism in the mother-child relationship. More contact and less negative encounters with mothers were also found for these children when compared with those of children on a placebo. In contrast, there was no difference in the amount of contact with fathers for those on medication versus placebo (Schachar et al., 1987).

### *Comparisons between Mother-Child and Father-Child Relationships*

Interactions in general between children and their parents have been shown to differ for mothers and fathers. When compared, mothers tend to be more directive & demanding as a result of spending more time with their children (Lytton, 1979), but they express more warmth towards their children (Buhrmester, Camparo, Christensen, Shapiro Gonzalez & Hinshaw, 1992). Fathers however, tend to have the role of being more playful and less directive (Lewis & Lamb, 2003). Much of the research into

parenting and psychopathology has focused on mothers as they are more often the primary caregiver (Belsky, 1979; Collins & Russell, 1991). Also, in clinical practice mother's report is most widely used as the parent rating, this is particularly so for ADHD which uses in general mother and teacher reports for diagnosis. However, there is an increasing amount of research which includes fathers (Phares & Compas, 1992). In their review of research of the father's role in child psychopathology, Phares and Compas (1992) showed fathers to be important in child psychopathology and that there were differences between fathers of children with ADHD compared with fathers of normal controls. The only community based study which specified both mother- and father-child relationships and ADHD found that child ADHD scores predicted low support from the father, but no reciprocal effect was found (Gadeyne et al., 2004). In contrast for the mother-child relationship, controlling parenting was shown to have a transactional association with children's ADHD symptoms (Gadeyne et al., 2004).

The results shown in the previous chapter also suggest that the association between ADHD symptoms and quality of parent-child relationship differs for the mother-child vs. the father-child relationship. Indeed no directional effects were found for ADHD symptoms and father-child hostility, whereas directional effects were found for mother-child hostility and ADHD symptoms (but only for males). Comparisons in this chapter were therefore drawn between mother- and father-child rejection to examine whether there are differences in the association with ADHD symptoms for this parent-child relationship dimension. Any variations in pattern of associations were directly compared for mothers vs. fathers.

A few studies in the clinical ADHD population have compared mother- and father-child relationships some of which found differences and others which did not (Tallmadge & Barkley 1983; Buhrmester et al., 1992; Arnold, O'Leary & Edwards

1997). Tallmadge & Barkley (1983) compared mother- and father-child interactions with hyperactive and normal boys. Parents of hyperactive children were found to be more commanding than those of normal children. Within the hyperactive boys group, parents' behaviour did not differ for mothers and fathers. However, the hyperactive boys responded with more negative and competing behaviour to their mothers' commands than controls, but there was no difference between hyperactive and control groups in response to fathers' commands (Tallmadge & Barkley 1983). In contrast, Buhrmester et al. (1992) found different parenting between mothers and fathers with their hyperactive sons. Both parents were more controlling than parents in the control group, but mothers of hyperactive sons tended to be more demanding than fathers. Mothers of hyperactive sons also showed more positive behaviours towards their sons than fathers did. Not only does this show differences between mothers' and fathers' parenting, but in situations where both parents were present relationships were different again with fathers becoming more demanding and mothers becoming less so, thus suggesting complex parent-child relationships in families with children with ADHD (Buhrmester et al., 1992). Finally, Edwards and colleagues (Edwards, Barkley, Laneri, Fletcher & Metevia, 2001) found that mothers of children with ADHD or ODD reported greater intensity of anger during conflict with their children than fathers did. Children's reports of their own behaviour indicated more hostility towards their mothers than fathers (Edwards et al., 2001).

### *Rejection in the Parent-Child Relationship*

The analyses within this chapter specifically compare the association of ADHD symptoms and rejection in the mother-child relationship with ADHD symptoms and rejection in the father-child relationship. An association between

parental rejection and children's behavior problems has been shown in previous studies (e.g. Shaw et al., 1998; Muris, Meesters & van den Berg, 2003; Roelofs, Meesters, ter Huurne, Bamelis & Muris, 2006). In a sample of young children Shaw et al. (1998) found that rejection from the mother was a significant predictor of externalizing behavior 18 months later. In a cross sectional sample of adolescents, Muris, Meesters and van den Berg (2003) showed a significant association between a number of dimensions of the parent-child relationship and externalizing behavior, however the strongest correlation was between externalizing and perceived parental rejection. More recently Roelofs, Meesters, ter Huurne, Bamelis and Muris (2006) also showed a significant relationship between both mother and father rejection and child aggression in a community sample of children aged 9 to 12 years old. Rohner's and colleagues' cross cultural work on parental acceptance-rejection theory also suggests negative outcome for children who receive parental rejection (Rohner, Khaleque & Cournoyer, 2005). Indeed Stern, Rohner and Sacks-Stern (2007) showed that in a sample of children with ADHD, acceptance as reported by mothers significantly predicted aggressive behaviour. Given that these research findings were not specifically examining ADHD symptoms, the present chapter examined how rejection in the parent-child relationship may be associated with ADHD symptoms.

#### *From Parent-Child Relationships to General Family Atmosphere*

The quality of the parent-child relationship has been examined to a great extent in terms of its impact upon children. The parent-child relationship and parenting have been key factors in studies and theories of child development (e.g. Baumrind, 1966; Bowlby, 1969) as well as being recognised as an intermediate factor through which inter-parental conflict exerts its effect on children (Erel & Burman,

1995). The parent-child relationship has therefore been a key focus in this thesis. However as mentioned in the introduction chapter, systems theory (Minuchin, 1985) suggests that the relationships within a family (and beyond in the wider system of social network, peers and community) are dynamic and influence each other. The effects of the overall atmosphere within the family may therefore have an impact on children's ADHD symptoms and similarly children's ADHD symptoms may have an effect on conflict within the family. This broader measure of family environment is therefore examined in this chapter. Previous studies examining this association are now discussed.

#### *Family Conflict and ADHD Symptoms*

Previous research using both clinical and community samples has shown mixed results for the association between family conflict and ADHD symptoms (Johnston & Mash, 2001). Family problems have been reported to exacerbate ADHD symptoms and families with ADHD are more likely to be conflicting (Ingram, Hetchman, & Morgenstern, 1999). Biederman et al. (1995a) also found that increasing numbers of family adversities as measured by Rutter's adversity indicators were associated with ADHD. Specifically examining family conflict, families of both boys and girls with ADHD have been found to have higher levels of family conflict than in control families (Biederman et al., 1995a; Biederman et al., 1995b; Biederman, Faraone & Monuteaux, 2002). In contrast however, Brown & Pacini (1989) found no difference in family conflict between families of boys with ADHD compared to clinical and non-clinical controls.

Community samples measuring ADHD at a trait level have also shown differing results. Lucia & Breslau (2006) found a significant positive association

between family conflict and ADHD at age 6 and 11 years (using the FES and CBCL). In contrast, George, Herman and Orstrander (2006) found a significant correlation between ADHD and family conflict, but once conduct problems and depression had been controlled for the relationship was no longer significant.

The studies discussed in this section have examined the general atmosphere within the family (as they used the FES which measures the social climate of the family; Toulitos, Perlmutter & Murray, 2001) rather than examining specific family relationships. The general nature of the measure may be a possible reason why some studies find no association. One of the aims in this chapter was therefore to assess this association in two community samples. Both cross sectional and longitudinal associations were examined. The hypothesis that family conflict is significantly associated with ADHD symptoms was tested. Where there was a significant association, bidirectional influences were expected. This is because a child with ADHD symptoms in the family may have an impact on the overall atmosphere in the family. Similarly, conflict within the family may have a negative impact upon the child and therefore exacerbate their ADHD symptoms (Ingram, Hetchman, & Morgenstern, 1999). Similar to coercive family processes there may be cyclical effects, although this theoretical idea is applicable to aggressive behaviours and conduct problems rather than ADHD symptoms.

### *The Present Chapter*

In this chapter the association between ADHD symptoms and mother-child and father-child rejection was examined over time (1 year). Next the association between ADHD symptoms and family conflict was examined. In the CaStANET this was across an eight year time period and in the SWFS across one year.

## Methods

### *Sample*

Both the CaStANET and SWFS were used for this study.

### SWFS

The SWFS included 309 families where at least one parent and the child had taken part at Time 1 and Time 2 (12 months later). There were 152 males and 157 females in the sample and they were aged between 11 and 14 years old ( $M = 11.68$  years at Time 1,  $SD = 0.47$ ,  $n = 309$ ). Because comparisons were drawn between the association of ADHD symptoms and the mother-child vs. father-child relationship, only cases where there was a mother and father report of their child's ADHD symptoms and where the child reported on both the mother and father-child relationship were included in the analyses of parent-child relationships ( $n = 256$  families where each family member responded). It was therefore possible to test for differences based on the same sample.

### *CaStANET*

A longitudinal sub-sample of the CaStANET, which included those where parents had completed questionnaires at both Time 1 (1996) and Time 2 (2004) was used. Due to the nature of the questions addressed in this chapter, only those families with twins under the age of 18 years at Time 2 were included ( $n = 165$  excluded). A further 20 families were excluded because the twins were not living together or with their parents. The total sample size for the longitudinal sub-sample in this chapter was therefore 552, however because of missing data on some of the constructs used, 488



participants were included in the analyses as they had complete data for ADHD and family conflict at both time points. At Time 1 the twins were aged between 5 and 11 years ( $M = 8.38$ ,  $SD = 1.41$ ) and at Time 2 they were aged between 12 and 17 years ( $M = 15.41$ ,  $SD = 1.37$ ). One twin was selected randomly (using the randomly assigned “twin 1” as detailed in Chapter 3) and this included 271 females and 281 males.

### *Measures*

#### *ADHD symptoms*

As described in the General Methods Chapter, children’s ADHD symptoms were measured using the attention problems subscale of the CBCL (Achenbach, 1991) in the SWFS. Both mother reports (MR) and father reports (FR) were used when respectively assessing the mother-child and father-child relationship. Scores were transformed using a square root transformation so that they approximated a normal distribution. In the CaStANET sample children’s ADHD symptoms were measured using the modified DuPaul scale (DuPaul 1991; Thapar et al., 2000). Parent reports (PR) were used (94% mother) in the present study. A log natural transformation was applied to normalise the ADHD scores. As described in the General Methods Chapter, the measures of ADHD in both samples showed good internal consistency.

#### *Family relationships*

Rejection in the mother- and father-child relationship was measured using the acceptance and rejection subscales of the CRPBI (Margolies & Weintraub, 1977). A log natural transformation was applied to the rejection scores.

The Family Environments Scale (Moos and Moos, 1976) was used to measure family conflict. In both the SWFS and CaStANET sample 9 items were used, however as detailed in the General Methods Chapter, they differed slightly (see Appendix II and V) on 2 items. Also in the SWFS children reported on family conflict whereas in the CaStANET parents reported on family conflict. Possible scores ranged from 0 to 9. These family relationship variables all showed good internal consistency (see General Methods Chapter).

### *Analyses*

Initially correlations between each family relationship variable and ADHD symptoms were computed. To assess the directional nature of the association between family relationships and ADHD symptoms, cross lagged panel and reciprocal effects models were fitted to the data using LISREL (LISREL 8.80; Jöreskog & Sörbom, 2006) as detailed in the General Methods Chapter. Stacked modelling was used to examine whether variation in the pattern of results for the mother-child vs. father-child relationship was significant.

## **Results**

### *Parent-Child Rejection and ADHD Symptoms*

Children's reports of rejection in their relationship with their mother and father were significantly different (Table 5.1). Both at Time 1 and Time 2 children reported that there was more rejection in the father-child relationship than in the mother-child relationship. At Time 2 fathers' reports of ADHD symptoms were significantly greater than mothers' reports. Correlations between ADHD scores and children's reports of rejection were significant for both mothers and fathers at Time 2,

but not at Time 1 (Table 5.1). Reciprocal effects and cross lagged models were fitted to the data. In the mother-child model ADHD scores (MR) significantly influenced rejection both across time and within time (Figure 5.1). However, mother-child rejection did not have a significant impact upon ADHD scores.

For fathers, a different pattern of effects was found. ADHD symptoms did not have an impact upon rejection, but rejection in the father-child relationship significantly influenced ADHD symptoms (FR) both across and within time (Figure 5.2). These results are interesting as they are contrary to the findings showing the effects of children's ADHD symptoms on mother-child rejection. The results for father-child rejection are consistent with family relationships having a risk effect on ADHD symptoms.

Because different patterns of association with ADHD symptoms were found for mother-child rejection and father-child rejection, these were further explored to determine whether the patterns were significantly different for mother-child rejection vs. father-child rejection. In order to compare the differences between the mother-child and father-child models, stacked modelling was used. These showed that the effect of ADHD symptoms at Time 1 on parent-child rejection at Time 2 was significantly greater in the mother-child model than the father-child model ( $\Delta\chi^2_{(1)} = 3.84, p = .05$ ). The pathway between parent-child rejection at Time 1 and ADHD symptoms at Time 2 was however not significantly different in the two models ( $\Delta\chi^2_{(1)} = 0.38, ns$ ). The reciprocal effect pathways showed marginal ( $p < .10$ ) differences when comparing the mother-child and father-child models. ADHD symptoms influencing parent-child rejection was marginally stronger in the mother-child model ( $\Delta\chi^2_{(1)} = 3.67, p < .10$ ) whereas the effect of parent-child rejection on ADHD

symptoms was marginally stronger in the father-child model compared with the mother-child model ( $\Delta\chi^2_{(1)} = 3.62, p < .10$ ).

**Table 5.1 Correlations between ADHD symptoms and rejection in the mother-child and father-child relationship across 12 months,  $n = 194$**

		Time 1 (1999)		Time 2 (2000)		Mean	SD
Mothers		ADHD	Rejection	ADHD	Rejection		
Time 1 (1999)	ADHD (MR)	-				1.46	.92
	Rejection	.12	-			2.92	.21
Time 2 (2000)	ADHD (MR)	.71**	.14*	-		1.33	.95
	Rejection	.28**	.51**	.29**	-	2.94	.23
Fathers		ADHD	Rejection	ADHD	Rejection	Mean	SD
Time 1 (1999)	ADHD (FR)	-				1.57 <sup>†</sup>	.89
	Rejection	.10	-			2.98 <sup>†</sup>	.23
Time 2 (2000)	ADHD (FR)	.66**	.18*	-		1.52 <sup>†</sup>	.94
	Rejection	.09	.54**	.22**	-	3.01 <sup>†</sup>	.24

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

<sup>†</sup> significantly greater mean ( $p < .05$ ) than for MR

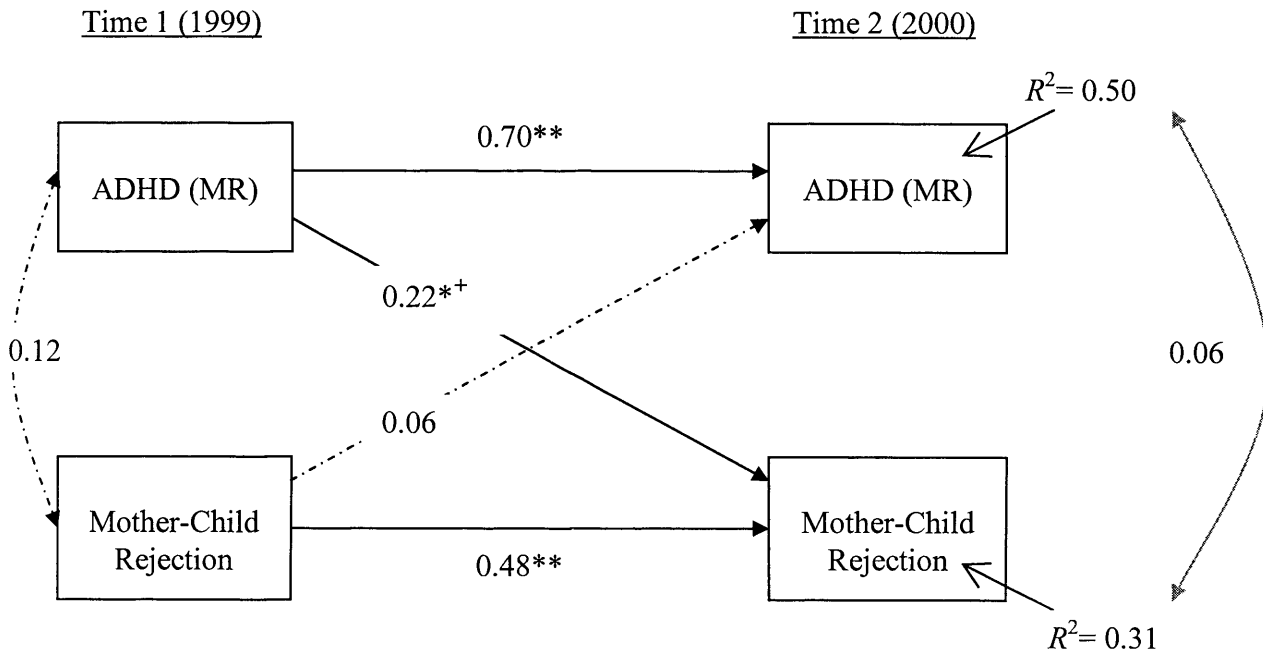
One possibility for the differences found for mothers and fathers in the association between parent-child rejection and ADHD symptoms could be partly due to the different reporters of ADHD symptoms. When reporting on their children's ADHD symptoms, mothers' and fathers' reports may have been capturing slightly different behaviours (indeed, the correlation between mother and father reporters of ADHD symptoms was less than 0.7). Because mother reports of ADHD symptoms are usually used rather than father reports, cross lagged and reciprocal effects models were therefore estimated using mother reports of ADHD symptoms and father-child rejection. None of the pathways between mother rated ADHD and father-child rejection were significant in the cross lagged model (Time 1 ADHD to Time 2

rejection  $\gamma = .11, t = 1.84, ns$ ; Time 1 rejection to Time 2 ADHD  $\gamma = .03, ns$ ) or reciprocal effects model (ADHD to rejection  $\beta = .14, t = 1.81, ns$ ; rejection to ADHD  $\beta = .02, ns$ ). This suggests therefore that the effect of father-child rejection on children's ADHD symptoms is specific to father reports of ADHD symptoms.

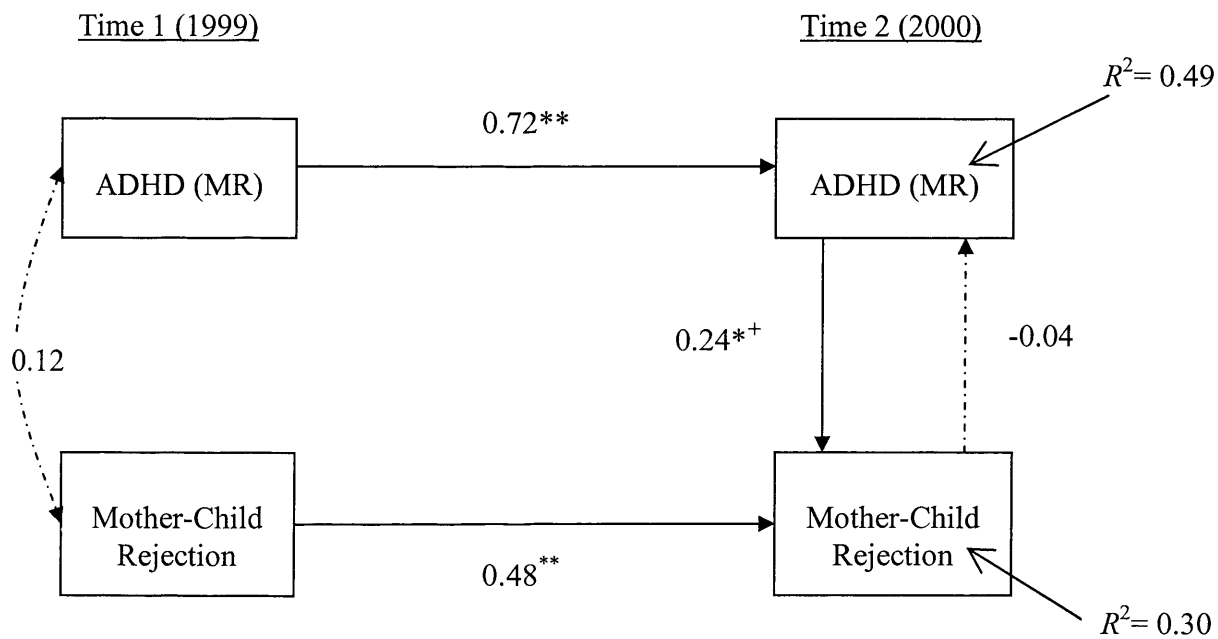
Models were also estimated using a composite ADHD score (average of MR and FR ADHD scores) so that ADHD symptoms captured by both parent reporters were included. Results showed bidirectional influences in the mother-child cross lagged model (Time 1 ADHD to Time 2 rejection  $\gamma = .22, p < .05$ ; Time 1 rejection to Time 2 ADHD  $\gamma = .15, p < .05$ ), but the reciprocal effects model showed an influence of ADHD on rejection ( $\beta = .19, p < .05$ ) and not the converse ( $\beta = .04, ns$ ). For fathers, similar results to the models using father report of ADHD were found in that father-child rejection had a significant influence on ADHD symptoms ( $\gamma = .10, p < .05$ ;  $\beta = .12, p < .05$ ) but ADHD symptoms did not impact upon rejection ( $\gamma = .07, ns$ ;  $\beta = .06, ns$ ). These results suggest that father reports of ADHD symptoms are perhaps indexing something slightly different to mother reports and these other symptoms are influenced by parent-child rejection.

**Figure 5.1 Maximum likelihood estimation of cross lagged (Panel A) and reciprocal effects (Panel B) models for ADHD symptoms and mother-child rejection, \* $p < .05$ , \*\* $p < .01$ , + significantly greater than father-child pathway,  $n = 194$**

**Panel A**



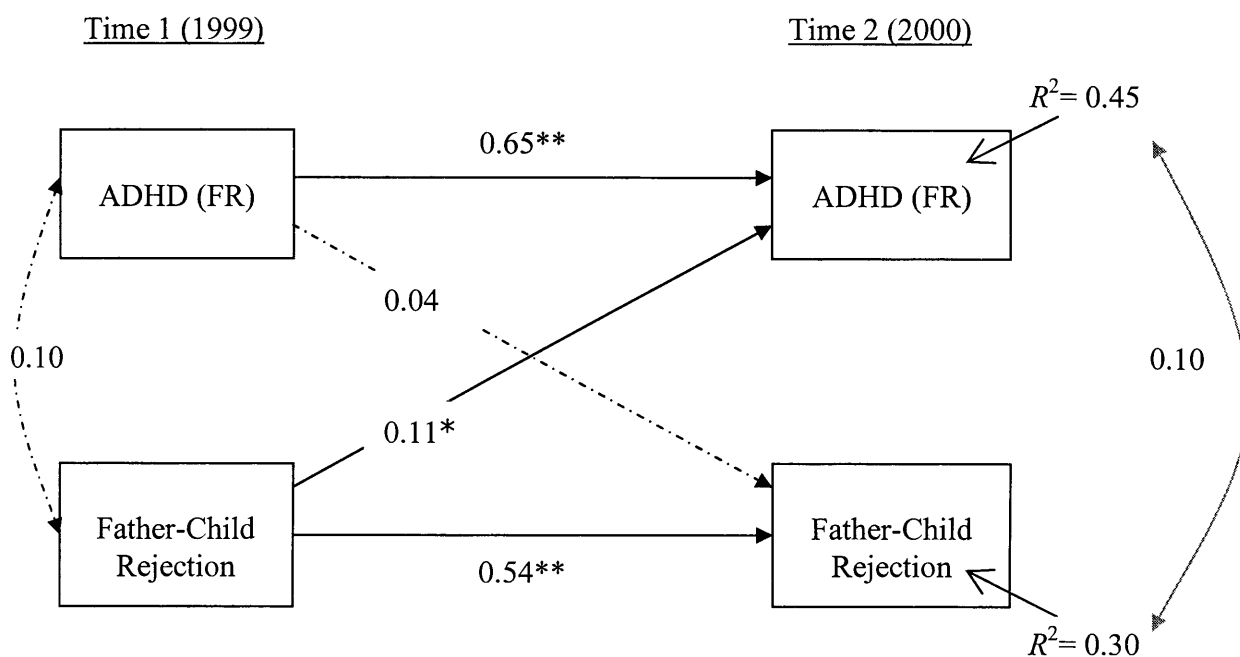
**Panel B**



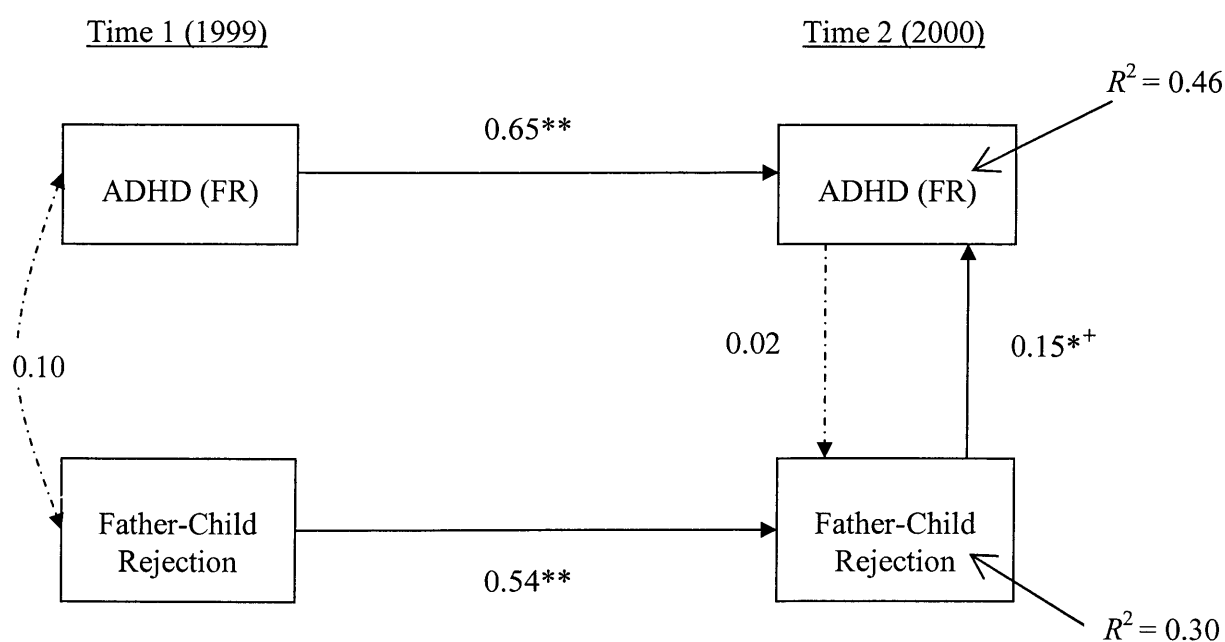
$\chi^2_{(1)} = 3.34$ , GFI = 0.99, AGFI = 0.91

**Figure 5.2 Maximum likelihood estimation of cross lagged (Panel A) and reciprocal effects (Panel B) models for ADHD symptoms and father-child rejection, \*  $p < .05$ , \*\*  $p < .01$ , + significantly greater than mother-child pathway,  $n = 194$**

**Panel A**



**Panel B**



$\chi^2_{(1)} = 0.61$ , GFI = 1.00, AGFI = 0.98

### Family Conflict and ADHD Symptoms

The association between family conflict and ADHD symptoms was assessed across one year in the SWFS sample. Means and standard deviations of both ADHD symptoms and family conflict are shown in Table 5.2. Father reports of ADHD symptoms were significantly greater than mother reports both at Time 1 and Time 2. Correlations between both mother and father reports of ADHD symptoms and family conflict were weak and non-significant ( $n = 225$ , range  $r = -.06$  to  $r = .09$ ,  $ns$ ; Table 5.2) therefore further analyses were not carried out. These results suggest that across a one year period family conflict and ADHD symptoms are not associated.

**Table 5.2 Correlations between ADHD symptoms and family conflict across 12 month in the SWFS,  $n = 225$ .**

		Time 1 (1999)		Time 2 (2000)		Mean	SD
Mothers		ADHD	Family conflict	ADHD	Family conflict		
Time 1 (1999)	ADHD (MR)	-				1.52	.91
	Family conflict	.08	-			3.23	2.13
Time 2 (2000)	ADHD (MR)	.74**	-.06	-		1.38	.96
	Family conflict	.02	.49**	-.02	-	3.16	2.21

		ADHD		Family conflict		Mean	SD
Fathers		ADHD	Family conflict	ADHD	Family conflict		
Time 1 (1999)	ADHD (FR)	-				1.62 <sup>†</sup>	.93
	Family conflict	.05	-			3.23	2.13
Time 2 (2000)	ADHD (FR)	.69**	.07	-		1.56 <sup>†</sup>	.95
	Family conflict	.03	.49**	.09	-	3.16	2.21

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

<sup>†</sup> significantly greater mean ( $p < .05$ ) than for MR



Next, the CaStANET sample was used to assess the association between ADHD symptoms and family conflict in the longitudinal sub-sample. Age was significantly correlated with ADHD scores both at Time 1 ( $r = -.09, p = .04, n = 488$ ) and at Time 2 ( $r = -.11, p = .02, n = 488$ ), but there was no significant correlation between age and family conflict (Time 1  $r = .02, ns, n = 488$ ; Time 2  $r = -.01, ns, n = 488$ ). Correlations between ADHD symptoms and family conflict, both reported by the parent, ranged from  $r = .13$  to  $.30$  (Table 5.3). ADHD symptoms at Time 1 had a significant impact upon family conflict at time 2, but the converse was not significant (Figure 5.3). Within Time 2, ADHD symptoms also had a significant impact on family conflict when taking initial levels of each variable into account at Time 1, but family conflict did not have an impact on ADHD symptoms. The reciprocal effects model was a good fit to the data ( $\chi^2_{(1)} = .45, p = .50, GFI = 1.00, AGFI = 1.00$ ). The results suggest therefore that the social climate, specifically conflict, within the family is affected by children's ADHD symptoms.

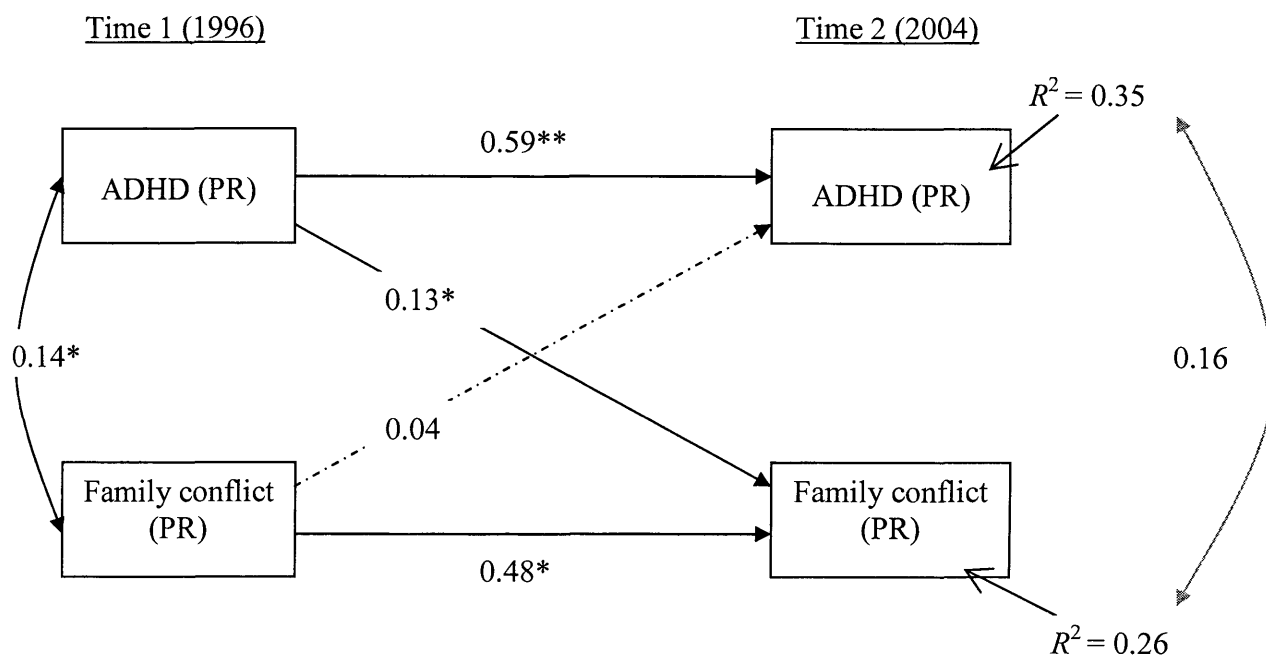
**Table 5.3 Correlations between ADHD symptoms and family conflict Time 1 and Time 2 in the CaStANET,  $n = 488$ .**

		Time 1 (1996)		Time 2 (2004)		Mean	SD
		ADHD	Family conflict	ADHD	Family conflict		
Time 1 (1996)	ADHD	-				2.25	.97
	Family conflict	.14**	-			3.12	2.20
Time 2 (2004)	ADHD	.59**	.13**	-		2.21	1.02
	Family conflict	.20**	.49**	.30**	-	2.92	2.28

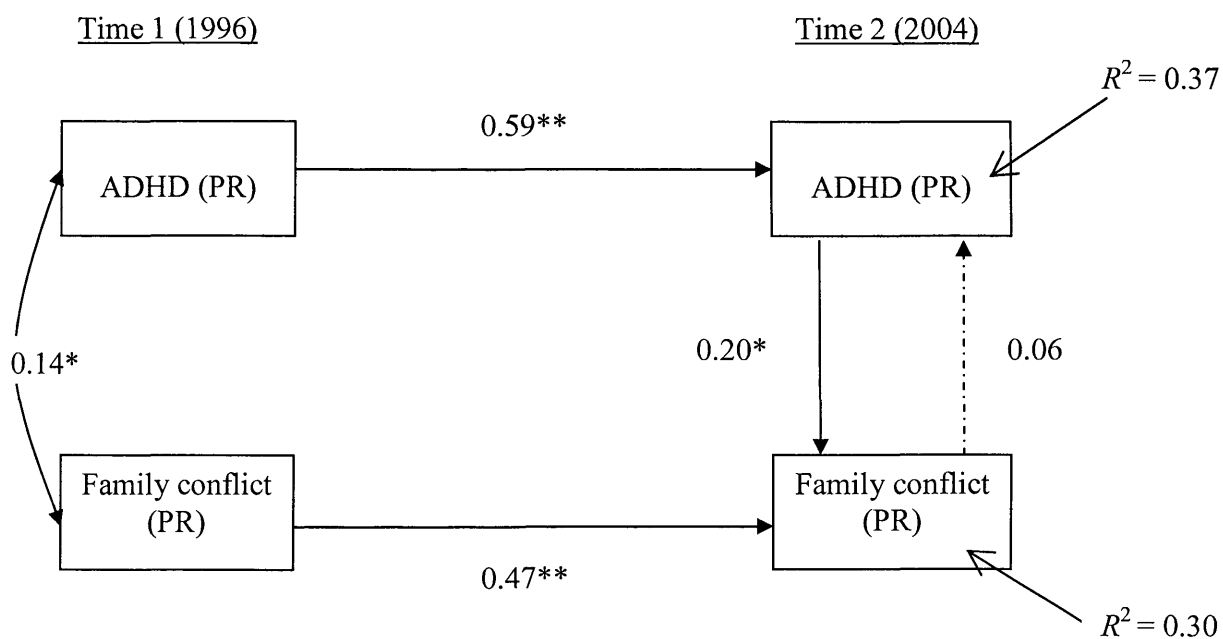
\*\*  $p < .01$

**Figure 5.3 Maximum likelihood estimation of cross lagged (Panel A) and reciprocal effects (Panel B) models for ADHD symptoms and family conflict across 8 years in the CaStANET,  $n = 488$**

**Panel A**



**Panel B**



$\chi^2_{(1)} = 0.45, GFI = 1.00, AGFI = 1.00$

The different findings in the two samples could come about for a number of reasons, such as the age ranges and the difference in reporter of family conflict. These will be discussed further in the main discussion. However, one other plausible reason why the effects of ADHD symptoms are apparent across the eight year time lag and when older adolescents are included, is that there may be cumulative effects of children's symptoms on conflict within the family. ADHD may have an initial effect on one family subsystem such as conflict within the parent-child relationship. Over time this may have a cumulative effect and impact upon the whole family. Indeed, as already detailed in the General Methods Chapter, family conflict shows moderate correlations with warmth, hostility and rejection in the parent-child relationship. While not testing directional hypotheses these associations support the idea that these family relationship factors may be influencing each other.

### *Summary of results*

There was a significant effect of ADHD symptoms on family conflict 8 years later as well as a significant impact of ADHD symptoms on rejection in the mother-child relationship. This effect of ADHD symptoms having an impact on mother-child rejection was significantly different to the respective pathway for fathers suggesting a greater impact of ADHD symptoms on mother-child rejection. Indeed, for fathers, rejection had a significant impact upon their children's ADHD symptoms and not vice versa. In contrast, no association was found between ADHD symptoms and family conflict across one year. Overall the results show most support for the hypothesis that ADHD symptoms have a detrimental effect on family relationships.

## **Discussion**

The aim of this chapter was to examine the associations between family relationship variables and ADHD symptoms over time that were not examined in Chapter 4. Parent-child rejection and a broad measure of social climate in the family (family conflict) were investigated. Both mother-child and father-child rejection were examined as a need for more research specifically including fathers has previously been highlighted (Phares & Compas, 1992). Differences between the associations for mother-child and father-child relationship and ADHD symptoms were also examined. The results were varied depending on the family relationship being examined, the sample being utilised, as well as by parent gender. Given the previous mix of findings this was not unexpected.

The association between ADHD symptoms and rejection showed a varying pattern of results for rejection in the mother-child relationship and the father-child relationship. ADHD symptoms were shown to have a significant impact on rejection in the mother-child relationship. This was shown both across time and within time after taking the stability of each variable into account which therefore suggests that the findings are robust. There was no evidence for rejection in the mother-child relationship having an impact upon ADHD symptoms. These results therefore support the idea first suggested by Bell (1968) of child effects on parents. Similarly the findings are consistent with treatment studies that have shown improvements in parent-child relationships when stimulant medication is used to successfully treat ADHD symptoms (e.g. Schachar et al., 1987). These are also consistent with the findings for boys' ADHD symptoms having an impact upon mother-son hostility shown in the previous chapter.

In contrast to rejection in the mother-child relationship, there was a significant effect of father-child rejection on children's ADHD symptoms both across and within time, but there was no significant effect of ADHD symptoms on father-child rejection. These findings are contrary to the notion of child effects on parent, and support psychological theory and research which emphasises the effects of parents and the parent-child relationship on their child's adjustment (e.g. attachment theory, Bowlby, 1969; parenting, Baumrind, 1966).

The effect of ADHD symptoms on rejection was significantly greater for mother-child rejection than for father-child rejection across time and marginally so ( $p < .10$ ) within time. The impact of ADHD symptoms on mother-child rejection therefore shows an absolute significant effect as well as a relative effect when compared with father-child rejection. The effect of rejection on ADHD symptoms was not significantly different for mothers and fathers across time, but within time showed a marginal difference. Specific hypotheses regarding differences in the association between mother-child and father-child rejection were not made and therefore these results must to an extent be taken as exploratory. However, as differences were found, possible explanations for these differences are discussed.

The finding that ADHD symptoms have a greater effect on mother-child rejection than father-child rejection may be partly due to different involvement parents have with their children. Mothers tend to spend more time with their children than fathers do and therefore are probably more involved in everyday activities with their children. Children's ADHD symptoms may be more problematic in task focused activities, such as getting ready for school and chores, and may therefore have an impact upon the mother-child relationship. In contrast, as fathers tend to interact with their children in more play activities, symptoms of ADHD may have less of an impact

upon their relationship as they are less relevant for the task in hand. The nature as well as the amount of interaction may play a role in the differential findings for mother-child and father-child rejection and the association with children's ADHD symptoms.

Another possibility is that the variation in findings for mother-child and father-child rejection is partly due to the different reporters of ADHD symptoms. Mother and father reports of ADHD symptoms were used in the respective mother-child and father-child models. The reports from the different parents may be tapping slightly different constructs and this could be contributing to the variation in findings. Inter-parental rater agreement on the CBCL however is reported to be good (Achenbach, 1991). The correlations between mother and father reports of ADHD symptoms were found to be moderate to high ( $r = .61$  to  $.66$ ,  $p < .01$ ,  $n = 194$  to  $233$ ) but were not as strong as those shown in normative data published for the CBCL (Achenbach, 1991). Because mother reports of ADHD symptoms are more frequently used in both clinical and research settings than father reports, the association of ADHD symptoms reported by the mother with father-child rejection (reported by the child) was also examined. The results showed no significant directional pathways, thus suggesting there may be some differences in results based on parent reporter. Also a composite of ADHD symptoms reported by both mother and father was examined in relationship to rejection and showed similar results to the original analyses except mother-child rejection influenced ADHD symptoms across time. This is unsurprising given this was the pathway that was not statistically different for mothers and fathers, but still suggests that fathers' reports of ADHD symptoms may be capturing other symptoms (which may be more affected by rejection) which mothers' reports do not.

Differences in parents' reports may be due to their perceptions of the child's behaviour or due to the child's expression of different behaviours with each parent respectively (and in perhaps differing situations). It was not possible to test these possibilities in the present study. For the analyses in this chapter, the reporter of ADHD symptoms was consistent with the person who the child was reporting on their relationship with. By using the different informants, the mother's or father's perceptions of their child's symptoms were assessed along with the child's perception of the specific parent-child relationship.

Having examined parent-child rejection, the association between conflict within the family and ADHD symptoms was next investigated. This showed that there was an association in the CaStANET sample but not in the SWFS. Not only was there a longitudinal association between family conflict and ADHD symptoms in the CaStANET, but the analyses suggested that ADHD symptoms were having a significant impact on conflict scores eight years later. Also, when controlling for the stability of both ADHD symptoms and family conflict, the direction of influence was from ADHD symptoms to family conflict and not the other way around. Because this association was found across quite a large time span (8 years), it is interesting that there was no association between family conflict and ADHD symptoms in the SWFS which was across a shorter amount of time. While the CaStANET sample was larger than the SWFS this does not appear to be the reason for the discrepancy in findings, as the magnitude of the correlations between ADHD symptoms and family conflict in the CaStANET was greater than in the SWFS. Possible reasons for the differences in the sample are suggested below.

Firstly, the difference in results for family conflict and ADHD symptoms in the two samples could be due to the difference in ages and the amount of time

between assessments in each of the samples. Those in the SWFS were all older children/younger adolescents at both time points, whereas those in the CaStANET were children at Time 1 and adolescents at Time 2. The impact of ADHD symptoms on family conflict could perhaps accumulate over time, and thus the SWFS does not show an association because those in the sample have not reached an age where the ADHD symptoms have an impact upon the whole family. The possibility that ADHD symptoms have a cumulative effect on family conflict over time is supported by the association being significant in the twin study across eight years, but not in the SWFS which was only across one year. Drawing on a family systems perspective, ADHD symptoms may have a negative impact on parent-child dyads initially, which over time have a detrimental effect on the wider family. Having examined specific aspects of the parent-child relationship and finding ADHD symptoms have an effect on them, this explanation, while not explicitly tested, seems plausible.

Alternatively, the differences between findings in the two samples may be partly due to the measurement properties of each sample. The ADHD measures were different for each sample and this may play a role in different findings. If the CBCL attention problems subscale measures more inattentive symptoms than overactivity symptoms than in the DuPaul, these hyperactivity symptoms may be having a greater effect on family conflict. However previous research has shown that the CBCL is a good screening tool for ADHD (Chen et al., 1994). Similarly, the family conflict subscale used two different items in each subscale, but given the good internal consistency of both measures it seems unlikely that a difference in two items would have much of an effect on the results. Perhaps more likely is the fact that in the CaStANET parents report on both variables, therefore the association could be affected by shared method variance. That is, the association between ADHD



symptoms and family conflict may be inflated because the same person reports on both constructs. Having said that, if this were the case there is no reason why there is only an effect in one direction between ADHD symptoms and family conflict, both associations should be affected to the same degree and therefore bidirectional effects would be expected.

The results from the analyses of family conflict therefore suggest that there is some evidence that ADHD symptoms have an impact on the overall social climate of the family (in this case family conflict). This appears to be over a long period of time and show effects in adolescence rather than over a short period of time in childhood and early adolescence. The results should be taken with some caution as they were not consistent across samples. In both samples however there was no evidence for conflict within the family having a significant influence on children's ADHD symptoms.

Drawing the results together from each of the family relationship variables there appears to be evidence for ADHD symptoms having an impact on some family relationships, namely mother-child rejection and family conflict. There was also a small amount of evidence for the effect of father-child rejection on ADHD symptoms. The variations in results across the different dimensions of parent-child relationship (rejection and both warmth and hostility as described in the previous chapter) are interesting and highlight the importance of investigating different aspects of the parent-child relationship.

### *Limitations*

A few limitations should be mentioned with regard to the analyses in this chapter. As expected in a study of ADHD symptoms, boys scored significantly higher than girls and therefore splitting the sample by child gender would have been

interesting. Also given the results of the previous chapter which showed a difference in the association between mother-child hostility and ADHD symptoms for boys and girls, analyses in the present chapter by child gender may have yielded different results. However, because parent gender was the focus of the present chapter this necessitated mother, father and child to have taken part, and therefore the sample size did not allow for also examining child gender.

Another limitation is that because of the restraint on including mother, father and child in the sample, the results were for those in two parent families and may not be generalisable to other family types. Relationships between parents and their children may differ when the child lives with one parent rather than two. Similarly the relationship between a parent and child who live together may differ to those who do not live together, thus the relationship between ADHD symptoms and parent-child relationships may also vary.

The final limitation as with all of the chapters in this thesis is that the findings may not generalise to clinical samples and therefore caution is noted.

### *Conclusions*

This chapter has shown that family relationship variables, both broad and specific, vary in their association with ADHD symptoms. No association was found in the SWFS between family conflict and ADHD symptoms. An effect of ADHD symptoms on family factors was found for both family conflict in the CaStANET sample and mother-child rejection in the SWFS, whereas father-child rejection was shown to have an effect on ADHD symptoms.

## **Chapter 6. General Discussion**

### **Introduction**

This thesis set out a number of aims in order to examine the role of both genetic and specific family relationship factors in the continuation of ADHD symptoms. These aims were addressed using two longitudinal community samples, one of which was also genetically informative. Possible causal effects of family relationship factors on ADHD symptoms were investigated both by examining the genetic and environmental mediation of the association between parent-child hostility and ADHD symptoms as well as by establishing the direction of influences between family relationship factors and ADHD symptoms. A discussion of the findings as a whole will now be presented followed by a discussion of the strengths and limitations of the thesis. To conclude implications for practice will be suggested.

### **Evidence of Family Effects on ADHD**

While genetic factors showed a considerable contribution to ADHD symptoms and their continuation, environmental influences were also shown to have an impact on stability and change in symptoms. Indeed, the majority of change in ADHD symptoms was due to non-shared environmental factors. The associations between ADHD symptoms and family relationship factors (family conflict, parent-child warmth, hostility and rejection) were explored in Chapters 4 and 5.

Other than father-child rejection there was no suggestion that the parent-child relationship dimensions examined in this thesis (warmth, hostility, rejection) or the more general measure of family conflict have a significant impact upon ADHD symptoms. Father-child rejection was therefore the exception. Here, there appeared a

significant effect on ADHD symptoms. It therefore seems that rejecting parenting from the father may have a detrimental effect on children in terms of their expression of ADHD symptoms. This finding from the longitudinal analyses is consistent with a causal hypothesis, however this effect could be genetically mediated, thus further research to establish whether this has an environmentally mediated effect is important. Research designs, such as a twin study which is genetically informative or an intervention study, are necessary to test for causality (Academy of Medical Sciences, 2007).

While father-child rejection was the only family relationship variable examined which showed a significant impact upon ADHD symptoms, this should not preclude further analyses of other family relationships. The evidence from the longitudinal twin analyses of significant non-shared environmental factors having an impact upon both the stability and change in ADHD symptoms supports the investigation of other environmental factors, which could include dimensions of family relationships that have not been examined in this thesis. Family factors, such as ineffective discipline or controlling parenting, could be explored. It is however also possible that family factors do not have a risk effect on ADHD symptoms. The analyses from this thesis highlight that examining different aspects of relationships and different genders as well as using different samples result in some variation in findings. Thus, it is necessary to test other potential family variables. Also replication of the findings from this thesis is necessary to have more confidence in them.

Some suggestions for why there was little evidence in this thesis for the effect of parent-child relationships on ADHD symptoms are warranted. One possibility could be that there was little or no effect of parent-child relationships on ADHD due to the nature of ADHD. Because ADHD is understood as a neurodevelopmental

disorder, the evidence suggested for genetic factors playing a large role in its aetiology may indeed be having a great influence. If ADHD symptoms arise because of biological, neurodevelopmental processes, there may be less scope for the quality of parent-child relationship to play a role than in other child behaviours which have a less biological basis. Previous research which has examined the association between parent-child relationships and children's behavioural adjustment has examined externalising behaviours or internalising symptoms. In contrast, the analyses in this thesis have looked specifically at ADHD type symptoms. This highlights the need to examine ADHD symptoms separately from other externalising behaviour problems such as CD and ODD as the evidence in this thesis suggests results may be different for ADHD.

### **Genetic Mediation of the Association between ADHD Symptoms and Family Relationships**

The initial genetic analyses of each of the family relationship variables which were genetically informative showed evidence of rGE, that is, there were substantial genetic influences on variation in parent-child hostility and warmth. There was one exception to this: for males there was no evidence of rGE for mother-son warmth, shared and non-shared environmental factors explained all of the variance. Not only was there evidence for genetic influences on parent-child relationships, but the association between both mother- and father-child hostility and ADHD symptoms was to a large extent genetically mediated. That is, the same genetic factors appear to influence both parent-child hostility and ADHD symptoms. Indeed, for father-child hostility and ADHD symptoms there was only evidence of a genetically mediated association.

The results showing genetic mediation highlight that this needs to be taken into consideration in other studies which examine parent-child relationships and ADHD symptoms. Where it is not possible for a study to be genetically informative a measure of parental ADHD symptoms could be included as this may partly control for genetic influences on the association between child ADHD symptoms and parent-child relationship. However the association between parental ADHD symptoms and parent-child relationships would first need to be established. Results from a study by Johnston and colleagues (2002) do not support this as they found no association between mothers' own childhood ADHD symptoms and their responsiveness in parent-child interactions (Johnston, Murray, Hinshaw, Pelham and Hoza (2002). In contrast, Psychogiou and colleagues (2007; 2008) found maternal ADHD symptoms to be associated with some aspects of parenting and not others. They also suggest interactive effects of parental and child ADHD symptoms on parenting, with differences for mothering vs. fathering (Psychogiou et al., 2008). This suggests there may be complex associations between parental and child ADHD symptoms and parenting. Thus, initially the use of genetically informative samples would be preferable to further examine the genetically mediated association between quality of parent-child relationship and ADHD symptoms rather than using parental ADHD symptoms as a way of accounting for this genetic association.

### **Evidence for ADHD Symptoms Affecting Family Relationships**

The effects of ADHD symptoms on mother-child rejection, mother-son hostility and family conflict all point towards the negative impact that these symptoms have not only on the child experiencing the symptoms but also on the family as a whole. Because this direction of effects was found across different aspects of family

relationships (both specific quality of parent-child relationship and overall family conflict) and in two different samples which used different measures of ADHD symptoms and had different time lags, the findings are remarkably consistent. The fact that the effect of boys' ADHD symptoms on mother-son hostility was environmentally mediated adds further support to the conclusion that boys' ADHD symptoms have a negative impact upon family environment as this relationship was still evident when genetic associations had been accounted for. Interventions to improve boys' ADHD symptoms could improve the relationship between mothers and sons (as suggested by treatment studies). Alternatively, parent training which perhaps help mothers to cope with their sons' symptoms and react in a less hostile manner may also improve their relationship with their sons.

Given that parent-child relationships have been shown to impact upon other aspects of children's behaviour such as conduct problems and oppositional defiance (e.g. Burt et al., 2005; Shelton et al., 2008), the parent-child relationship may be an important factor through which ADHD symptoms have a negative impact upon these other behavioural outcomes (Johnston et al., 2002). The negative impact that ADHD symptoms have upon family relationships therefore is an important area of outcome for children with ADHD which would merit intervention. Outcomes such as anti-social behaviour and conduct disorder may then also be affected by improvements in family relationships.

The impact that ADHD symptoms have upon the more global family conflict construct may also impinge upon the adjustment of other children in the family. Taking a systems approach to understanding the family as made up of a number of dynamic relationships, necessitates an awareness of the potential implication of not only ADHD symptoms on quality of parent-child relationships and family social

climate, but also the effects that these relationship constructs may have upon other relationships within the family. Exploring these wider impacts of the parent-child relationship and family conflict on the family was beyond the scope of this thesis but in light of the findings will be important to consider. Future research could focus on other family relationships, such as parent-parent and sibling-sibling, as well as parent-child relationships to gain a more complete picture of the impact ADHD symptoms have on the whole family.

The analyses in this thesis aimed to examine more proximal measures of family environment than general psychosocial adversity. While family conflict (FES, Moos & Moos, 1976) used in the previous chapter (in the longitudinal analyses of the SWFS and CaStANET) represented a more general measure of family environment than the specific measures of parent-child relationship quality, it can still be regarded as a more proximal measure of family environment than psychosocial adversity. Family conflict has been included as a measure of psychosocial adversity in some previous research (Biederman et al., 1995a; Biederman, Faraone & Monuteaux, 2002). Biederman and colleagues (2002), found a measure of family conflict (which included the conflict, cohesion and expressiveness subscales of the FES) to be associated with ADHD status. When the family conflict measure was included as part of the psychosocial adversity composite, risk for ADHD increased with number of adversities (Biederman et al., 2002). While these measures of family environment included both past month and past year ratings, the study (Biederman et al., 2002) was cross sectional and therefore it is not clear as to the direction of these associations. It is interesting therefore that when examining just one of these adversity factors the effect is found in the direction of ADHD symptoms having an impact upon family environment. The psychosocial adversity scale which Rutter (1976) initially used within



a longitudinal design to examine the effects on children's psychiatric outcome included marital discord rather than family conflict. Therefore the FES (including conflict) measure used by Biederman and colleagues (Biederman et al., 2002) may not be indexing marital discord and therefore should not be included in a composite of psychosocial adversity. Biederman et al. (1995a) suggest that the FES construct may be measuring some different aspects of family environment than just marital discord. It therefore seems important to distinguish between these family adversity factors (family conflict and marital conflict) even when using a composite measure of psychosocial adversity.

### **Examination of Gene-Environment Interaction**

Because there was no evidence of an environmentally mediated effect of quality of parent-child relationship on ADHD symptoms, there was no evidence to suggest these parent-child dimensions should be used to examine possible GxE. Had father-child rejection been measured in the twin study and shown evidence of environmental mediation, this would have been a good candidate. But with all of the other measures of aspects of the parent-child relationship and overall conflict within the family, there was no evidence of them being risk factors for ADHD. Previous studies which have examined GxE for ADHD with family factors being the environmental factor should therefore perhaps be treated with some caution. However none of these specifically examined the quality of parent-child relationship as the environmental factor interacting with a genotype and influencing ADHD. Laucht et al. (2007) and Retz et al. (2008) used a measure of childhood or psychosocial adversity. Laucht and colleagues (2007) included quality of marital partnership rather than family conflict in a composite of psychosocial adversity whereas Retz and

colleagues (2008) included violence, delinquency and chronic conflict in a measure of emotional family climate which formed part of their childhood adversity measure.

Waldman (2007) used marital stability as the environmental factors in his study of GxE effects on ADHD. In contrast, while Sheese et al. (2007) used a measure of parenting quality (including supportiveness, respect for autonomy, stimulation of cognitive development, hostility and confidence) in their GxE study, their outcome measure was child temperament rather than ADHD.

These first few studies may be suggesting gene-gene interaction effects rather than GxE. That is, because there may be genetic influences on the environmental risk factors, as supported by the findings of this thesis, what appears to be GxE may indeed be gene-gene interaction. Future studies are therefore needed which focus on environmental factors which have a causal effect on ADHD. Once established as environmental risk factors, studies can then investigate evidence for GxE. However, from the findings in this thesis, family conflict, mother-child rejection and mother-son hostility are not aspects of family relationships which should be explored for GxE studies.

## **Gender Differences**

A number of gender differences were found across the studies. Mean levels in ADHD symptoms were different for males and females. This is consistent with previous studies which have shown a male preponderance in ADHD diagnosis as well as males having higher mean ADHD scores in community samples (Gaub & Carlson 1997; Taylor et al., 1998). No evidence was found for gender differences in the contribution of genetic and environmental factors on ADHD symptoms, either cross sectionally or longitudinally. In contrast there was evidence of gender differences in

the proportion of variance explained by genetic and environmental factors for both warmth and hostility in the mother-child relationship. The gender differences in association between ADHD symptoms and some dimensions of the parent-child relationship are perhaps unsurprising. Firstly, differences in the mother-child and father-child relationship in general have been suggested (Collins & Russell, 1991; Lewis & Lamb, 2003). Secondly, in terms of child gender, because levels of ADHD tend to be greater for boys than girls some differences in the association may be expected. Because the results for mother-child hostility in the longitudinal analyses showed an effect of boys' ADHD symptoms on mother-son hostility this highlights the need to use larger samples that allow researchers to split the sample by gender so that results for male and female children as well as mothers and fathers can be compared. Further exploration of the gender differences was not possible due to sample size.

### **Different Dimensions of the Parent-Child Relationship**

While the variation in findings for different genders has been discussed, findings were also different across dimensions of the parent-child relationship (rejection, warmth and hostility). No or very low association was found between ADHD symptoms and warmth. Hostility however was shown to be associated, but the only directional association was from sons' ADHD symptoms to mother-son hostility. In contrast, rejection was associated with ADHD for both mothers and fathers, but the direction of effects were opposite. This highlights the importance of investigating different aspects of the parent-child relationship. While the measures of family conflict were correlated (as shown in the General Methods Chapter), the correlations were not so high that they are indexing the same constructs. Some discussion as to

why these different dimensions of the parent-child relationship may be associated differently with ADHD symptoms is now provided.

The rejection and acceptance items that were included in the parent-child rejection dimension tended to be related to practical situations and specific responses of parents to their children's behaviour. For example, the items 'forgets to help me when I need it' and 'makes me feel better when I am upset' are both specific to times when the child is in need of help or is upset respectively. Because they are interaction specific and in response to the child's situation or behaviour they may have a stronger association with children's ADHD symptoms. For mothers in particular their children's ADHD symptoms may decrease the mothers' capacity to respond in a positive and accepting manner and this may arise from constant organising for their child and the need for more supervision and encouragement to stay on task. Because fathers spend less time with their children their child's symptoms may impact upon them less, and the effect that rejection from the father has on the child may be more detrimental because the limited time they have to spend together is more precious. If interaction specific it may also be that the rejection may appear more directed at the child.

The hostility measure includes general feelings and behaviours of the parent towards the child and thus may be more characteristic of the parent in general. Hostility from the parent may therefore be less affected by children's ADHD symptoms than rejection. This is consistent with the idea already discussed that mother-son hostility may be particularly important rather than hostility in any other parent-child relationship because boys' ADHD symptoms were worse than girls' and may therefore have crossed a threshold for having an effect on hostility (which with other levels of ADHD symptoms may not be influenced). However, the instructions to

the children completing the rejection scale indicate that children should think about their general relationship with their mum and dad, whereas the hostility scale asks specifically about time spent with their parents in the last month and the frequency of parent's behaviour during that time. This therefore suggests that children may be reporting on specific times of interaction with their parent in the hostility measure but for their general relationship with their mother and father in the rejection measure.

Parent-child warmth and ADHD symptoms may not be associated due to the high skew of the variable. That is, such a large proportion of children reported a great deal of warmth there may not have been enough variation to show an association between ADHD symptoms and parent-child warmth. All children tended to score quite well on this scale and this therefore does not seem to be associated with children's symptoms.

These possible reasons for the variation in findings for the different dimensions of parent-child relationship are just suggestions and future research is needed to explore the reasons for the differences in more detail.

## **Strengths and Limitations**

A number of strengths and limitations have been highlighted in each individual chapter. Some of these are highlighted here, especially those which are relevant to every chapter and therefore to this thesis as a whole.

### *Reporter Effects*

In the twin study only one parent reported on their children's behaviour, the majority being mothers. In the SWFS however both mothers and fathers reported on their child. As discussed in Chapter 5, differences in reporters may partly explain the

differences in associations between mother-child and father-child relationship and ADHD symptoms. The use of father reports of ADHD symptoms is less common, and these could therefore tap into some other behavioural phenotype, alternatively they may be able to add something meaningful to the assessment of ADHD symptoms. Indeed the logic for using specifically either mother or father reports in Chapter 5 was so that the person who the child was reporting on their relationship quality with was the same person reporting on the child's ADHD symptoms. This was done with the assumption that the parents' report of the child's behaviour is what they will be responding to in the parent-child relationship, just in the same way that the child reports of the parent-child relationship quality are specific to each parent. Also, as discussed in Chapter 4, the attributions which parents have about their children's behaviour may differ both based on parent gender (Chen, Seipp & Johnson, 2008) and on child gender (Maniadaki, Sonuga-Barke & Kakouros, 2005). Therefore understanding the reason for reporter differences is important for understanding the possible mechanisms through which ADHD symptoms have an impact on the quality of parent-child relationship.

The use of children's perceptions of the parent-child relationships could be seen as a limitation as there is some evidence that children's perceptions of relationships may be affected by their ADHD symptoms (Gerdes, Hoza & Pelham, 2003). A study by Gerdes, Hoza and Pelham (2003) showed that children with ADHD reported more positively on their parent-child relationships than their parents did. Children's reports of parent-child relationship quality were however used in this thesis for two reasons. Firstly, children's perceptions of family relationships have been shown to be important for understanding the effects that these relationships have on children (Harold, Fincham, Osborne & Conger, 1997). Secondly, children's reports

of aspects of the parent-child relationship were used to decrease problems with shared method variance. That is, different reporters of the child's behaviour and the family relationship variables were used wherever possible so that associations between these factors were not inflated due to the same person reporting on both. Using different reporters ensures that the variables are independently measured and therefore this is a strength of the analyses.

### *Sample Differences*

Differences between the two study samples could also be regarded as a limitation. The measure of ADHD symptoms used in each sample was different and therefore may have been capturing slightly different constructs. However, as already mentioned in previous chapters, the CBCL attention problems subscale has been shown to be a good screening tool for ADHD (Chen et al., 1994) and to be associated with other measures of ADHD (Derks et al., 2008). The differences in the family relationship measures were small. Only two items on the family conflict scale were different, but the hostility and warmth measures were the same.

The age differences in the two samples could also account for some of the differences as discussed in Chapter 5. Despite the differences in sample ages and measures however there was considerable consistency in findings. Because consistent findings were shown in two different samples with different measures and age groups, this reinforces the results.

### *Sample Size*

Even though the sample sizes were considerable in both studies, the SWFS sample was not large enough to assess both parent gender and child gender in the

longitudinal analyses. Given the variation in findings for both parent and child gender it would have been interesting to have been able to compare across the four different parent-child dyads (by both parent and child gender). In comparison to the SWFS, the twin study had a much larger sample but measures of the quality of parent-child relationship were not included at the previous time point and only one parent (in most cases the mother) reported on children's ADHD symptoms, therefore it was not possible to conduct longitudinal analyses of the parent-child relationship factors.

Ideally if there had been a sample which was both longitudinal and genetically sensitive which included all of the specific relationship quality measures and included both parents, some of these questions regarding gender specific associations could have been addressed. Again though, the inclusion of two different samples with slightly different advantages, designs, measures and ages of participants can also be regarded as an advantage as the use of these can be seen as complementary, especially where findings are consistent between them.

### *Comorbid Conduct Problems*

Within this thesis the role of conduct problems was not examined, nor were they included as a covariate in the analyses. This was primarily because the aims of this thesis were focused specifically on ADHD symptoms. This could however, be regarded as a limitation to this thesis. As discussed in the introduction, ADHD shows high rates of comorbidity with other problems, especially ODD and CD. Not only this but some previous studies examining the association between family relationships and externalising behaviours have shown stronger associations of family relationships with conduct and oppositional problems than with ADHD symptoms. That is, in a study by Lindahl (1998) when split into three groups ADHD & ODD, ADHD only



and neither, parent-child relationships were worse in the ADHD & ODD group and significantly different to the control group, but the ADHD group was not different to either. Thus the ODD behaviours appeared to be playing a large role in the association between ADHD and negative family relationships. However, when examined, family relationships have been shown to have a negative impact upon children's adjustment, often operationalised as internalising (anxiety and depression) or externalising (delinquent and aggressive behaviours) rather than the opposite direction of effects. In light of the findings of this thesis (which show a different direction of effects), the importance of examining ADHD separately is highlighted.

#### *ADHD Subtypes*

A similar potential limitation is that subtypes of ADHD were not explored. Again, this was because ADHD symptoms as a whole were the primary focus of this thesis. Some studies have however investigated the inattentive and hyperactive/impulsive subtypes separately. For example, in their twin study Larsson, Lichtenstein and Larsson (2006), examined the genetic and environmental influences on ADHD subtype symptoms in a longitudinal analysis. Not only did they find genetic influences which influenced both subtypes, but they also found subtype specific influences. Interestingly, they also found evidence to suggest that there were significant gender differences in the proportion of variance explained by genetic and environmental factors. McLoughlin, Ronald, Kuntsi, Asherson and Plomin (2008) also used a twin study to examine the different subtypes of ADHD and similar to Larsson and colleagues (2006) found a large amount of genetic influences shared between the subtypes as well as some subtype specific influences. Future studies could therefore specifically examine the role of the subtype symptoms and their

association with family relationships. However, using ADHD symptoms as one construct has been an important first step. Having said this, because the research in this thesis has highlighted the importance of examining different aspects of the parent-child relationship, this should be a priority for future research before starting to examine the associations with different ADHD subtypes.

### *Generalisation*

Another limitation to the studies in this thesis, which has been mentioned briefly in the discussion sections of each of the main chapters, is the generalisation of the results. There are two considerations of the generalisability firstly, family type and secondly, the community nature of the samples. These will be addressed in turn. Due to the nature of the questions addressed within Chapters 3 and 4 the samples included children and adolescents from a range of different family types. That is, some were from two parent families (both biological and non-biological) and others from single parent families. In contrast, in order to draw direct comparisons between results for mother- and father-child relationship quality and ADHD in Chapter 5, the analyses included the same families and therefore the sample included only two parent families. It is possible that associations between ADHD symptoms and quality of parent-child relationship may differ in single parent households as well as with parents with whom the child does not live. The use of other samples which can explore these possible differences would be important for future research.

The second issue regarding the generalisability of the findings is the community nature of the samples. While ADHD has been shown to act as a dimensional construct, for clinical purposes there is a cut off. As this cut off includes only the extreme scorers of a positively skewed distribution, in community studies,

such as those utilised for this thesis, only a small proportion of children will have ADHD symptoms at a clinical level. Indeed, for both samples those who took part tended to have lower ADHD scores than those who only took part at a previous wave of data collection (see Chapter 2). There is the possibility that associations between family relationships and ADHD differ in a clinical population. While the community nature of the sample is a potential limitation in terms of generalisation to a clinical population, the fact that some of the results are consistent with results from clinical studies (Barkley & Cunningham, 1979; Schachar et al., 1987) indicates that there are similarities in community and clinical samples.

#### *Other Family Relationships*

As already mentioned in this discussion, other family relationships (parent-parent or sibling-sibling) were not included in the analyses in this thesis. Drawing from a family systems understanding of family relationships and their impacts upon children, these other relationships are important for the functioning of the family. Indeed, as family relationships are dynamic and interdependent, examination of the effects of ADHD symptoms and changes in the parent-child relationship on other family relationships is another important avenue for research.

#### **Practice Implications**

Notwithstanding the limitations, a number of practical implications arise from the findings in this thesis. Firstly, with regards to the effect of ADHD symptoms on the parent-child relationship, it is important for clinicians to assess these possible adverse effects on families. These could then be monitored along with treatment of ADHD symptoms. Where the quality of parent-child relationship does not improve

with treatment of the children's ADHD symptoms other interventions should perhaps be explored. Not only is it important for clinicians to be aware of the effects of children's ADHD symptoms on particularly the mother-child relationship, it is also important that the parents themselves are aware of this. Parenting stress felt by parents of children with ADHD could perhaps be compounded by the fact that parents may feel that they are partially to blame for their children's ADHD symptoms. The knowledge that their child's ADHD symptoms may impact upon their relationship with their child may help them to be aware of this during their interactions with their children and could help them to react in a less rejecting or hostile manner towards their child.

The results from this thesis also suggest that rejection in the father-child relationship has an impact upon children's ADHD symptoms. The inclusion of fathers in parent training programmes therefore appears vital. Efforts by clinicians and therapists to tailor parenting courses to both mothers and fathers may prove important. This could include not only specifically targeting father-child relationships, particularly rejection, but also practical things such as scheduling parenting classes in the evenings when fathers are more likely to be able to attend (Fabiano, 2007).

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## **Appendix I: CaStANET Twin Similarity Questionnaire (Completed by parents)**

**Twin Similarity Questionnaire (Cohen, Dibble, Grawe & Pollin, 1975; Nichols & Bilbro, 1966)**

This section will help us understand how much the twins have in common. Please circle yes or no.

### Response scale

1 = Yes

2 = No

- 1. Do the twins share the same natural hair colour?**
- 2. Do the twins share the same eye colour?**
- 3. Do the twins look alike as two peas in a pod?**
- 4. Do parents, brothers and sisters have trouble telling them apart?**
- 5. Is it hard for strangers to tell them apart?**
- 6. Are the twins identical?**

## Appendix II: CaStANET Parent Questionnaire

### ADHD Symptoms, DuPaul scale (1991)

About your twin's activity and concentration

Please circle the answer that best describes your first-born twin's behaviour during the *past three months*.

#### Response Scale

1 = Not at all

2 = Just a little

3 = Pretty much

4 = Very much

1. Often fidgets or squirms in seat
2. Has difficulty remaining seated
3. Is easily distracted
4. Has difficulty awaiting turn in groups
5. Often blurts out answers to questions
6. Has difficulty following instructions
7. Has difficulty sustaining attention to tasks
8. Often shifts from one uncompleted task to another
9. Has difficulty in playing quietly
10. Often talks excessively
11. Often interrupts or intrudes on others
12. Often does not seem to listen
13. Often loses things necessary for tasks
14. Often engages in physically dangerous activities without considering consequences
15. Restless or overactive
16. Excitable, impulsive
17. Disturbs other children/young people
18. Fails to finish things he/she starts – short attention span
19. Demands must be met immediately, easily frustrated
20. Cries often and easily
21. Mood changes quickly and drastically
22. Temper outbursts, explosive and unpredictable violent behaviour
23. Often runs about or climbs when he/she shouldn't be doing so
24. Often makes careless mistakes or does not pay attention to details
25. Often avoids or greatly dislikes tasks that require concentration
26. Often forgetful
27. Constantly fidgeting
28. Inattentive, easily distracted

## Family Conflict, Family Environment Scale (Moos & Moos, 1976)

This last section contains statements about families.

Please read each statement carefully and decide how well it describes your own family (who you live with now). You may feel that some of the statements are true for some family members and false for others. If so, please answer according to your best overall impression for your family.

### Response Scale

1 = Strongly disagree

2 = Disagree

3 = Agree

4 = Strongly agree

Please circle one number for each question.

1. In times of crisis we can turn to each other for support
2. Planning family activities is difficult because we misunderstand each other
3. We cannot talk to each other about the sadness we feel
4. Individuals are accepted for what they are
5. We avoid discussing our fears and concerns
6. We can express our feelings to each other
7. There are lots of bad feelings in the family
8. We feel accepted for what we are
9. Making decisions is a problem for our family
10. We are able to make decisions about how to solve problems
11. We don't get along well together
12. We confide in each other
13. Family members really help and support one another
- 14. We fight a lot in our family**
15. We often seem to be spending time at home
- 16. Family members rarely become openly angry**
17. We put a lot of energy into what we do at home
- 18. Family members sometimes get so angry they throw things**
19. There is a feeling of togetherness in our family
- 20. Family members hardly ever lose their tempers**
21. We rarely volunteer when something has to be done at home
- 22. Family members often criticise one another**
23. Family members really back each other up
- 24. Family members sometimes hit each other**
25. There is very little group spirit in our family
- 26. If there's a disagreement in our family, we try hard to smooth things over and keep the peace**
27. We really get along well with each other
- 28. Family members often try to one-up or out-do each other**
29. There is plenty of time and attention for everyone in our family
- 30. In our family, we believe you don't ever get anywhere by raising your voice**

## Appendix III: CaStANET Twin Questionnaire

### **Mother-Child Warmth and Hostility (Melby et al., 1993)**

#### You and Your Mum

Please complete the following questions for the person who is most like a mum to you.

This person is my... Mum      Step-mum      Dad's partner  
other.....

During the *past month* when you and your Mum have spent time talking or doing things together, how often did your Mum....

#### Response Scale

- 1 = Never
- 2 = Almost never
- 3 = Not too often
- 4 = About half
- 5 = Fairly often
- 6 = Almost always
- 7 = Always

- 1. Let you know she really cares about you**
- 2. Get angry at you**
- 3. Criticise you or your ideas**
- 4. Shout at you because she was upset with you**
- 5. Act loving and affectionate toward you**
- 6. Get into an argument with you**
- 7. Let you know that she appreciates you, your ideas or the things you do**
- 8. Help you do something that was important to you**
- 9. Argue with you whenever you disagreed about something**
- 10. Act supportive and understanding toward you**

## **Father-Child Warmth and Hostility (Melby et al., 1993)**

### You and Your Dad

Please complete the following questions for the person who is most like a dad to you.

This person is my... Dad    Step-dad    Mum's partner  
other.....

During the *past month* when you and your Dad have spent time talking or doing things together, how often did your Dad...

### Response Scale

- 1 = Never
- 2 = Almost never
- 3 = Not too often
- 4 = About half
- 5 = Fairly often
- 6 = Almost always
- 7 = Always

- 1. Let you know he really cares about you**
- 2. Get angry at you**
- 3. Criticise you or your ideas**
- 4. Shout at you because he was upset with you**
- 5. Act loving and affectionate toward you**
- 6. Get into an argument with you**
- 7. Let you know that he appreciates you, your ideas or the things you do**
- 8. Help you do something that was important to you**
- 9. Argue with you whenever you disagreed about something**
- 10. Act supportive and understanding toward you**

## Appendix IV: SWFS Parent Questionnaire

### Attention Problems, Child Behaviour Checklist (Achenbach, 1991)

#### Your Child's Behaviour

Below is a list of items that describe children and youth. For each item that describes your child now or within the past 6 months, please circle the 2 if the item is very true or often true of your child. Circle the 1 if the item is somewhat or sometimes true of your child. If the item is not true (as far as you know) of your child, circle the 0. Please answer all the items as well as you can, even if some do not seem to apply to your child.

#### Response Scale

0= Not True

1= Sometimes True

2= Very True

- 1. Acts too young for his/her age**
2. Argues a lot
3. Bragging, boasting
- 4. Can't concentrate, can't pay attention for long**
- 5. Can't sit still, restless, or hyperactive**
6. Clings to adults or too dependent
7. Complains of loneliness
- 8. Confused or seems to be in a fog**
9. Cries a lot
10. Cruelty, bullying or meanness to others
- 11. Day-dreams or gets lost in his/her thoughts**
12. Demands a lot of attention
13. Destroys his/her own things
14. Destroys things belonging to his/her family
15. Disobedient at home
16. Disobedient at school
17. Doesn't get along with other kids
18. Easily jealous
19. Fears he/she might think or do something bad
20. Feels he/she has to be perfect
21. Feels or complains that no one loves him/her
22. Feels others are out to get him/her
23. Feels worthless or inferior
24. Gets in many fights
25. Gets teased a lot
- 26. Impulsive or acts without thinking**
27. Would rather be alone than with others
- 28. Nervous, highly-strung, or tense**
- 29. Nervous movements or twitching**
30. Not liked by other kids
31. Too fearful or anxious

- 32. Feels too guilty
- 33. Overweight
- 34. Physically attacks people
- 35. Poor school work**
- 36. Poorly co-ordinated or clumsy**
- 37. Prefers being with younger kids
- 38. Refuses to talk
- 39. Screams a lot
- 40. Secretive, keeps things to self
- 41. Self-conscious or easily embarrassed
- 42. Showing off or clowning
- 43. Shy or timid
- 44. Stares blankly**
- 45. Stubborn, sullen or irritable
- 46. Sudden changes in mood or feelings
- 47. Sulks a lot
- 48. Suspicious
- 49. Talks too much
- 50. Teases a lot
- 51. Temper tantrums or hot temper
- 52. Threatens people
- 53. Underactive, slow moving or lacks energy
- 54. Unhappy, sad or depressed
- 55. Unusually loud
- 56. Withdrawn, doesn't get involved with others
- 57. Worries



## Appendix V: SWFS Child Questionnaire

### **Family Conflict, Family Environment Scale (Moos & Moos, 1976)**

These statements are about families. If you think a statement is true or mostly true about your family, or members of your family, circle 'T'. If you think a statement is false or mostly false about your family, circle 'F'. Remember, we would like to know what your family seems like to you.

#### Response Scale

True

False

1. Family members really help and support each other.
2. Family members often keep their feelings to themselves
3. **We fight a lot in our family**
4. We often seem to have a lot of time on our hands at home
5. We say anything we want to around the house.
6. **Family members rarely become openly angry**
7. We put a lot of energy into what we do at home
8. It's hard to 'blow off steam' at home without upsetting somebody.
9. **Family members sometimes really lose their temper.**
10. There is a feeling of togetherness in our family
11. We tell each other our personal problems
12. **Family members hardly ever lose their tempers**
13. We rarely volunteer when something has to be done at home
14. If we feel like doing something on the spur of the moment, we often just pick up and do it
15. **Family members often criticise each other**
16. Family members rarely back each other up
17. Someone usually gets upset if you complain in our family
18. **Family members sometimes shout at each other**
19. There is very little group spirit in our family
20. Money and paying bills is very openly talked about in our family
21. **If there's a disagreement in our family, we try hard to smooth things over and keep the peace.**
22. We really get along well with each other.
23. We are usually careful about what we say to each other
24. **Family members often try to outdo each other.**
25. There is plenty of time and attention for everyone in the family.
26. There are a lot of spontaneous discussions in our family.
27. **In our family, we believe you don't ever get anywhere by raising your voice**

## **Mother-Child Warmth and Hostility (Melby et al., 1993)**

During the past month when you and your mum have spent time talking or doing things together, how often did your mum...

### Response Scale

- 1= Always
- 2= Almost Always
- 3= Fairly Often
- 4= About Half
- 5= Not too Often
- 6= Almost Never
- 7= Never

- A. Get angry at you**
- B. Let you know she really cares about you**
- C. Criticise you or your ideas**
- D. Shout at you because she was upset with you**
- E. Act loving and affectionate toward you**
- F. Let you know that she appreciates you, your ideas or the things you do**
- G. Help you do something that was important to you**
- H. Get into an argument with you**
- I. Argue with you whenever you disagreed about something**
- J. Act supportive and understanding toward you**
- K. Insult or swear at you
- L. Call you bad names
- M. Tell you she loves you

### **Father-Child Warmth and Hostility (Melby et al., 1993)**

During the past month when you and your dad have spent time talking or doing things together, how often did your dad...

#### Response Scale

- 1= Always
- 2= Almost Always
- 3= Fairly Often
- 4= About Half
- 5= Not too Often
- 6= Almost Never
- 7= Never

- A. Get angry at you**
- B. Let you know he really cares about you**
- C. Criticise you or your ideas**
- D. Shout at you because he was upset with you**
- E. Act loving and affectionate toward you**
- F. Let you know that he appreciates you, your ideas or the things you do**
- G. Help you do something that was important to you**
- H. Get into an argument with you**
- I. Argue with you whenever you disagreed about something**
- J. Act supportive and understanding toward you**
- K. Insult or swear at you
- L. Call you bad names
- M. Tell you he loves you

**Child Report of Parent Behaviour Inventory (CRPBI; Margolies & Weintraub, 1977)**

**YOU AND YOUR MUM AND DAD**

Nowadays children may live in very different types of families. This part of the questionnaire asks about how you and your mum and dad get along. If you only live with one parent, you may feel that you cannot answer the questions about the other parent. If so, just answer for the parent you live with. Each sentence is an example of how a parent might get along with his or her child. Please read each sentence and describe how true it is of the way your mum or dad get along with you. My mum and dad...

Response Scale

True  
Sort of true  
Not true

1. **Makes me feel better after talking over my worries**
2. **Almost always speaks to me with a warm and friendly voice**
3. **Smiles at me very often**
4. **Makes me feel better when I am upset**
5. **Enjoys doing things with me**
6. **Cheers me up when I am sad**
7. **Often speaks of the good things that I do**
8. **Seems proud of the things I do**
9. Often makes me feel that he/she loves me
10. Always listens to my ideas and opinions
11. Often praises me
12. Is happy to see me when I come home from school or
13. Hugged or kissed me goodnight when I was small
14. Is very interested in what I am learning at school
15. Often makes me feel that I make him/her happy
16. **Isn't very patient with me**
17. **Forgets to help me when I need it**
18. **Is always nagging me**
19. **Almost always complains about what I do**
20. **Gets cross and angry about little things I do**
21. **Doesn't help me**
22. **Doesn't seem to know what I need or want**
23. Doesn't talk to me very much
24. Spends very little time with me
25. Doesn't seem to think of me very often
26. Doesn't show me that he/she loves me
27. Doesn't share many activities with me
28. Complains that I get on his/her nerves
29. Is always finding fault with me

30. Wishes I were a different kind of person
31. Sees to it that I know exactly what I may or may not do
32. Believes in having a lot of rules and sticking to them
33. Believes that all my bad behaviour should be punished in some way
34. Insists that I must do exactly what I am told
35. I have certain jobs to do and am not allowed to do anything else until they are done
36. Is very strict with me
37. Sticks to the rule instead of allowing a lot of exceptions
38. Gives hard punishments
39. Sees to it that I obey when he/she tells me something
40. Has more rules that I can remember, so is often punishing me
41. Usually doesn't find out about my misbehaviour
42. Doesn't pay much attention to my misbehaviour
43. Doesn't check up to see whether I have done what he/she told me
44. Seldom insists that I do anything
45. Does not bother to enforce rules
46. Is easy with me
47. Lets me off easy when I do something wrong
48. Excuses my bad conduct
49. Does not insist that I obey if I complain or protest
50. Can be talked into things easily
51. Doesn't tell me what time to be home when I go out
53. Gives me as much freedom as I want
54. Lets me go any place I want
55. Lets me go out any evening I want
56. Lets me do anything I like to do
57. Soon forgets a rule he/she has made
58. Punishes me for doing something one day, but ignores it the next day
59. His/Her mood determines whether a rule is enforced or not
60. Only keeps rules when it suits him/her
61. Changes his/her mind to make things easier for himself /herself
62. Will only talk to me when I displease him/her
63. Sometimes when he/she disapproves, he/she doesn't say anything but is cold and distant for a while
64. Is less friendly with me if I don't see things his/her way
65. Will avoid looking at me when I've disappointed him/her
66. If I've hurt his/her feelings he/she stops talking to me until I please him/her again