

# Psychological Medicine

<http://journals.cambridge.org/PSM>

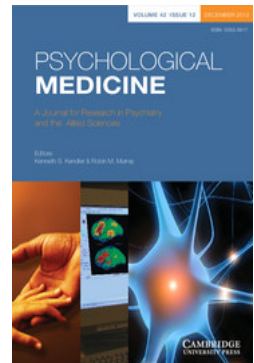
Additional services for **Psychological Medicine**:

Email alerts: [Click here](#)

Subscriptions: [Click here](#)

Commercial reprints: [Click here](#)

Terms of use : [Click here](#)



---

## Developmental associations between traits of autism spectrum disorder and attention deficit hyperactivity disorder: a genetically informative, longitudinal twin study

M. J. Taylor, T. Charman, E. B. Robinson, R. Plomin, F. Happé, P. Asherson and A. Ronald

Psychological Medicine / *FirstView* Article / November 2012, pp 1 - 12

DOI: 10.1017/S003329171200253X, Published online:

**Link to this article:** [http://journals.cambridge.org/abstract\\_S003329171200253X](http://journals.cambridge.org/abstract_S003329171200253X)

### How to cite this article:

M. J. Taylor, T. Charman, E. B. Robinson, R. Plomin, F. Happé, P. Asherson and A. Ronald Developmental associations between traits of autism spectrum disorder and attention deficit hyperactivity disorder: a genetically informative, longitudinal twin study. *Psychological Medicine*, Available on CJO doi:10.1017/S003329171200253X

**Request Permissions :** [Click here](#)

# Developmental associations between traits of autism spectrum disorder and attention deficit hyperactivity disorder: a genetically informative, longitudinal twin study

M. J. Taylor<sup>1\*</sup>, T. Charman<sup>2</sup>, E. B. Robinson<sup>3</sup>, R. Plomin<sup>4</sup>, F. Happé<sup>4</sup>, P. Asherson<sup>4</sup> and A. Ronald<sup>5</sup>

<sup>1</sup> Centre for Research in Autism and Education, Department of Psychology and Human Development, Institute of Education, University of London, London, UK

<sup>2</sup> Department of Psychology, Institute of Psychiatry, King's College London, London, UK

<sup>3</sup> Analytic and Translational Genetics Unit, Massachusetts General Hospital, Boston, MA, USA; Department of Medicine, Harvard Medical School, Boston MA, USA

<sup>4</sup> King's College London, MRC Social, Genetic and Developmental Psychiatry Centre, Institute of Psychiatry, De Crespigny Park, London, UK

<sup>5</sup> Genes Environment Lifespan Laboratory, Centre for Brain and Cognitive Development, Department of Psychological Sciences, Birkbeck College, University of London, London, UK

**Background.** Autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD), and associated subclinical traits, regularly co-occur with one another. However, the aetiology of their co-occurrence remains poorly understood. This paper provides the first genetically informative, longitudinal analysis of the interaction between traits of ASD and ADHD, and explores their genetic and environmental overlap.

**Method.** Parents of approximately 5000 twin pairs completed questionnaires assessing traits of ASD and ADHD when twins were aged 8 and 12 years. Cross-lagged longitudinal modelling explored their developmental association, enabling a consideration of phenotypic-driven processes. Overlapping aetiological influences on traits at age 12 years were explored using bivariate twin modelling.

**Results.** Traits of ADHD at age 8 years were more strongly predictive of traits of ASD at 12 years than traits of ASD at 8 years were of traits of ADHD at 12 years. Analysis of traits by subscales assessing specific symptom domains suggested that communication difficulties were most strongly associated with traits of ADHD. Bivariate modelling suggested moderate genetic overlap on traits in males (genetic correlation = 0.41), and a modest degree of overlap in females (genetic correlation = 0.23) at age 12 years.

**Conclusions.** Traits of ADHD at age 8 years significantly influence traits of ASD at age 12 years, after controlling for their initial relationship at age 8 years. In particular, early ADHD traits influenced later communication difficulties. These findings demonstrate the dynamic nature of co-occurring traits across development. In addition, these findings add to a growing body of literature suggesting that traits of ASD and ADHD may arise via similar aetiological processes.

Received 3 April 2012; Revised 24 September 2012; Accepted 1 October 2012

**Key words:** Attention deficit hyperactivity disorder, autism, longitudinal, twin study.

## Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental condition characterized by difficulties with reciprocal social interaction and communication, and the presence of repetitive, stereotyped behaviours and interests. ASD regularly co-occurs with other psychiatric and neurodevelopmental disorders; upwards of

70% of individuals with ASD meet diagnostic criteria for an additional psychiatric or neurodevelopmental disorder (de Bruin *et al.* 2007; Simonoff *et al.* 2008). Attention deficit hyperactivity disorder (ADHD) is particularly common; 28–60% of individuals meeting criteria for ASD also meet diagnostic criteria for ADHD (Yoshida & Uchiyama, 2004; Simonoff *et al.* 2008), and subclinical traits associated with these conditions show considerable covariation in the general population (Ronald *et al.* 2008). While the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; APA, 2012) will introduce changes, current diagnostic criteria (APA, 2000) do not

\* Address for correspondence: M. J. Taylor, M.Sc., Centre for Research in Autism and Education, Department of Psychology and Human Development, Institute of Education (University of London), 25 Woburn Square, London WC1H 0AA, UK.  
(Email: M.Taylor@ioe.ac.uk)

allow dual diagnosis of these conditions, and their co-occurrence hence remains poorly understood.

Behavioural genetic research has recently investigated whether shared genetic and environmental risk factors underlie ASD and ADHD. Findings from family studies are inconsistent. Nijmeijer *et al.* (2009) reported that ADHD and traits of ASD were genetically independent of one another. Conversely, Mulligan *et al.* (2009) reported that 56% of the phenotypic correlation between ADHD and ASD could be attributed to shared familial influences.

Twin studies have more consistently found evidence for overlapping genetic influences between these conditions and their related subclinical traits. With the possible exception of early childhood (Ronald *et al.* 2010a), when it can be more challenging to assess traits related to ASD and ADHD, twin studies suggest that traits of ASD and ADHD share considerable genetic influences when assessed in middle childhood (Ronald *et al.* 2008; Lichtenstein *et al.* 2010; Lundström *et al.* 2011), early adolescence (Lichtenstein *et al.* 2010; Lundström *et al.* 2011), early adulthood (Reiersen *et al.* 2008) and adulthood (Lundström *et al.* 2011), and share a modest degree of environmental influences (Reiersen *et al.* 2008; Ronald *et al.* 2008).

Despite the developmental nature of ASD and ADHD, longitudinal studies of their association are lacking. Longitudinal designs enable questions surrounding causality to be addressed in terms of how the phenotypes of interest influence one another across development. One study to date has used longitudinal methods to examine the developmental association between traits of ASD and ADHD. St Pourcain *et al.* (2011) used latent class growth analysis to explore the association of social-communication traits and traits of ADHD across development. They found that children with persistently impaired social-communicative abilities were either moderately or persistently impaired on hyperactive-inattentive behaviours. Additionally, children with persistent hyperactive-inattentive symptoms displayed more persistent social and communication difficulties.

No twin research to date has adopted longitudinal methods to explore the association between traits of ASD and ADHD. Cross-lagged modelling is a form of twin modelling that considers the direct influence of multiple phenotypes on one another across development while controlling for their concurrent association at an earlier age (Burt *et al.* 2005). The model also estimates genetic and environmental influences on each trait at each specified age, as well as their genetic and environmental overlap. The model also shows the proportion of genetic and environmental influences that are transmitted across time, and the proportion that are unique to each age. While cross-lagged

modelling has been used to explore other behaviours in childhood (e.g. Burt *et al.* 2005; Hallett *et al.* 2010; Greven *et al.* 2011), we are the first to explore phenotypic-driven processes as they relate to ASD and ADHD using this method.

We aimed to explore longitudinal associations between traits of ASD and ADHD between the ages of 8 and 12 years using cross-lagged modelling. We specifically focused on the period between the ages of 8 and 12 years due to the important developmental changes that occur across this period, as the transition from childhood to adolescence begins. We aimed to assess the direct influence of traits of ASD on traits of ADHD across this period, as well as the reverse association to explore the bidirectional causal relationship across development. Given the putative 'fractionable' nature of the core symptoms of ASD (Happé *et al.* 2006; Ronald *et al.* 2006; Happé & Ronald, 2008) and evidence for some genetic specificity within traits of ADHD (McLoughlin *et al.* 2007; Asherson & Gurling, 2012), we also fitted cross-lagged models to measure subscales exploring associations between specific symptom domains of ASD and ADHD. St Pourcain *et al.* (2012) provided evidence to suggest a dynamic relationship between traits across development; hence we expected that traits of ASD and ADHD would significantly influence one another across development. Given the lack of genetically informative, longitudinal research regarding the association of traits of ASD and ADHD, we did not have specific hypotheses concerning the relative strengths of the associations.

Additionally, we aimed to estimate the degree of genetic and environmental overlap across traits of ASD and ADHD by applying bivariate twin model fitting to data at age 12 years. Ronald *et al.* (2008) reported bivariate twin models for traits of ASD and ADHD when the sample used in the present study were aged 8 years. With the advantage of using the same sample and the same measures as this previous study, we aimed to explore the extent to which common genetic and environmental influences operate on traits of ASD and ADHD when the twins were aged 12 years. We expected traits of ASD and ADHD to show moderate genetic overlap, and a modest degree of environmental overlap.

## Method

### *Participants*

Parents of twins participating in the Twins Early Development Study (TEDS) completed questionnaires regarding their twins' traits of ASD and ADHD. TEDS is a community sample of twins born in England and

**Table 1.** Scores for each of the scales at both ages, split by zygosity

Zygosity	CAST age 8			Conners age 8			CAST age 12			Conners age 12		
	<i>n</i> <sup>a</sup>	Mean	(s.d.)	<i>n</i> <sup>a</sup>	Mean	(s.d.)	<i>n</i> <sup>a</sup>	Mean	(s.d.)	<i>n</i> <sup>a</sup>	Mean	(s.d.)
Monozygotic male	891	5.49	(3.53)	888	12.81	(9.49)	972	5.25	(3.78)	920	11.81	(9.31)
Monozygotic female	1053	4.33	(2.97)	1053	9.41	(8.34)	1163	4.27	(3.16)	1120	8.20	(7.59)
Dizygotic male	819	5.71	(3.68)	817	12.69	(9.92)	934	5.38	(3.73)	862	11.43	(9.47)
Dizygotic female	910	4.60	(2.98)	911	9.33	(8.08)	1025	4.55	(3.14)	987	8.55	(7.72)
Dizygotic opposite sex	1683	5.25	(3.52)	1680	10.76	(9.23)	1889	5.24	(3.62)	1779	9.92	(8.74)

CAST age 8, 31-item Childhood Autism Spectrum Test at age 8 years; Conners age 8, Conners' Parent Rating Scale at age 8 years; CAST age 12, 30-item Childhood Autism Spectrum Test at age 12 years; Conners age 12, Conners' Parent Rating Scale at age 12 years; s.d., standard deviation.

<sup>a</sup> Frequency of the sample by zygosity and sex is given by the number of twin pairs.

Wales between 1994 and 1996 (Oliver & Plomin, 2007). Data were collected when twins were aged 8 and 12 years. A total of 6762 families returned questionnaires when twins were aged 8 years, while 7520 were returned at age 12 years. Participants were excluded if they displayed specific medical syndromes, such as Down's syndrome or Fragile X, and chromosomal abnormalities. Exclusions also included extreme perinatal complications, unavailable zygosity data, lack of informed consent, missing birth order details, and unavailable first contact data. A total of 1406 twin pairs were excluded at age 8 years and 1537 were excluded at age 12 years. The final sample comprised 5356 twin pairs at the age of 8 years and 5983 twin pairs at the age of 12 years. Zygosity was determined by DNA testing and parental report (Goldsmith, 1991), which has been shown to be 95% as accurate as DNA testing (Price *et al.* 2000). Sample frequencies by zygosity are presented in Table 1. Written informed consent was provided prior to completion of the questionnaires.

## Measures

### Traits of ASD

Parents completed the Childhood Autism Spectrum Test (CAST; Scott *et al.* 2002) at both ages. The CAST comprised 31 items at age 8 years and 30 items at age 12 years (due to the removal of an age-inappropriate item). Questions concern behaviours associated with ASD in children, and are answered 'yes' or 'no'. The maximum score is 31; those scoring 15 or above are defined as 'at risk' of ASD (Williams *et al.* 2005). The CAST provided an overall score and, in-line with prior studies (Ronald *et al.* 2006, 2010b), was also broken down into three subscales corresponding to Diagnostic and Statistical Manual of Mental Disorders, fourth edition, text revision (DSM-IV-TR)

subcategories of ASD symptoms: (a) social, (b) communication, and (c) repetitive, restrictive behaviours/interests (RRBI). The CAST displayed good internal consistency (age 8 years:  $\alpha=0.71$ ; age 12 years:  $\alpha=0.73$ ).

### Traits of ADHD

Traits of ADHD were rated by parents at both ages using the ADHD subscale of the Conners' Parent Rating Scale (Conners) (Conners *et al.* 1998). The scale includes 18 items, which correspond closely to DSM-IV-TR symptom criteria for ADHD. Parents rated the extent to which each statement is true of their child on a four-point scale (maximum score = 54). As well as an overall ADHD symptom score, the scale data were divided into two subscales corresponding to the two ADHD symptom domains: hyperactivity/impulsivity and inattention. The Conners displayed excellent internal consistency ( $\alpha=0.91$  at both ages).

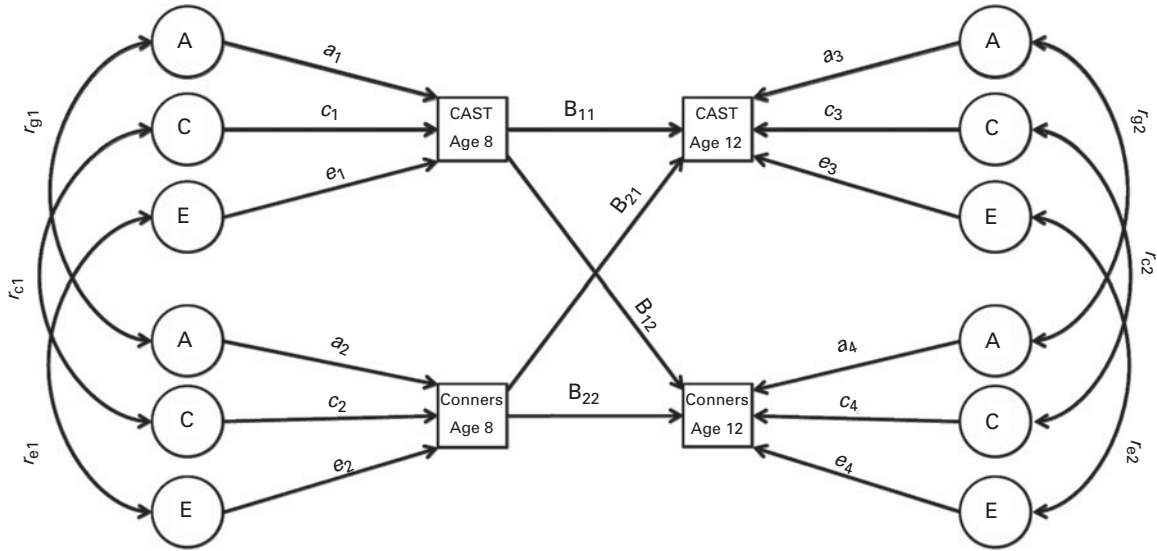
## Data analysis

### Data preparation

The CAST and Conners scales were log-transformed for positive skew to meet with the assumptions of twin modelling. The effects of sex and age were regressed out of the CAST and Conners scales in line with standard behavioural genetic procedures, and analyses were conducted on residual scores.

### Correlations

Cross-trait cross-twin (CTCT) intraclass correlation coefficients (ICCs) are the foundation of bivariate twin modelling. These correlate one twin's CAST score with their co-twin's Conners score, and cannot exceed the phenotypic correlation between traits. Using SPSS (SPSS Inc., USA), the CTCT ICCs were obtained



**Fig. 1.** Example cross-lagged path diagram. A, C and E are latent variables that estimate the degree of additive genetic (A), shared environmental (C) and non-shared environmental (E) influences operating upon each trait individually at each age. The additive genetic ( $r_g$ ), shared environmental ( $r_c$ ) and non-shared environmental ( $r_e$ ) correlations indicate the proportion of these influences that are shared across traits at each age. Longitudinal associations are indexed by parameters labelled  $B_{11}$ ,  $B_{12}$ ,  $B_{22}$  and  $B_{21}$ .  $B_{11}$  and  $B_{22}$  are stability effects, and indicate the extent to which each trait is stable across development.  $B_{12}$  and  $B_{21}$  are cross-lagged pathways, which are partial regression coefficients that assess the influence of each trait on the other across time. Stability and cross-lagged parameter estimates are influenced by the pre-existing associations of traits at 8 years. CAST age 8, 31-item Childhood Autism Spectrum Test at age 8 years; CAST age 12, 30-item Childhood Autism Spectrum Test at age 12 years; Conners age 8, Conners' Parent Rating Scale at age 8 years; Conners age 12, Conners' Parent Rating Scale at age 12 years.

separately for monozygotic (MZ) and dizygotic (DZ) twins. MZ twins share 100% of their DNA code, while DZ twins share approximately 50% of their DNA code (Hall, 2003). Consequently, genetic influences on the phenotypic correlation are implied if the MZ ICC exceeds the DZ ICC. Since MZ twins are genetically identical, any within-pair MZ differences are caused environmentally. Hence, if the MZ ICC is less than the phenotypic correlation, the presence of non-shared environmental influences, which create differences between twins and include measurement error, on the covariance between traits is suggested. Shared environmental influences create cross-twin similarity, and are implicated if the DZ ICC is greater than half the MZ ICC. These correlations were computed across trait scores at each age and across age groups.

#### Bivariate twin model fitting at age 12 years

Bivariate twin model fitting estimates parameters corresponding to additive genetic ('A'), shared environmental ('C') and non-shared environmental ('E') influences for each trait. The 'genetic correlation' ( $r_g$ ) estimates genetic overlap between traits;  $r_g$  falls between  $-1$  and  $1$ . If  $r_g = 1$  or  $-1$ , all genetic influences are shared between two traits, while  $r_g = 0$  indicates no

shared genetic influences. Shared environmental ( $r_c$ ) and non-shared environmental ( $r_e$ ) correlations are also computed and operate in the same fashion. Such a model is termed the 'ACE' model or Cholesky decomposition, and was fitted using Mx (Neale *et al.* 2003). AE, CE, and E models that constrained certain parameters to equal zero, enabling an assessment of their significance, were fitted in addition to the ACE model. Quantitative sex differences were tested with sex limitation models, which provide separate parameter estimates for males and females. This model was fitted without the inclusion of DZ opposite-sex twins.

#### Cross-lagged modelling between the ages of 8 and 12 years

Cross-lagged modelling explored longitudinal associations. Fig. 1 presents an example cross-lagged path diagram. A, C and E are estimated for each trait at each age, as well as  $r_g$ ,  $r_c$  and  $r_e$ . At the second age, these are residual correlations, and hence may differ from estimates derived in a bivariate model at one age only.  $B_{11}$  and  $B_{22}$  are stability pathways, and assess the effect of each trait at the age of 8 years on the same trait at the age of 12 years.  $B_{12}$  and  $B_{21}$  are cross-lagged pathways, and estimate the direct influence of traits of

ASD at the age of 8 years on traits of ADHD at the age of 12 years ( $B_{12}$ ), and vice versa ( $B_{21}$ ). Stability and cross-lagged pathways are partial regression coefficients that assess the direct influence of traits at the age of 8 years on traits at the age of 12 years whilst accounting for their pre-existing association at the age of 8 years (Burt *et al.* 2005). The model estimates the percentage of variance in each trait unique to age 12 years and that which is shared across ages, which is further decomposed into that due to A, C and E influences on each trait and their covariance at the age of 8 years. All parameters within the cross-lagged model were estimated separately for males and females, with the exception of  $r_g$ ,  $r_c$  and  $r_e$ , which were constrained to be equal across sexes due to the inclusion of opposite-sex DZ twins (Neale *et al.* 2006). Models were fitted to full-scale CAST and Conners scores, and measure subscales. These models explored associations between CAST subscales and the overall Conners scale (CAST social-Conners, CAST RRBI-Conners, CAST communication-Conners), Conners subscales and overall CAST scale (Conners hyperactivity/impulsivity-CAST, Conners inattention-CAST), and six models exploring the association of each of the three CAST subscales with the two Conners subscales. Models were also fitted controlling for the effects of a composite 'g' score, which assessed general cognitive ability, and both with and without individuals with confirmed or suspected ASD included. Cross-lagged models were fitted using Mx (Neale *et al.* 2003).

To compare the cross-lagged model with an alternative explanation of the covariance between traits across development, the fit of the model was compared with that of a longitudinal Cholesky decomposition. The longitudinal Cholesky model is an extension of the bivariate model detailed above, and contained four variables: CAST at age 8 years, Conners at age 8 years, CAST at age 12 years and Conners at age 12 years. The model provides A, C and E estimates for each of the four variables, as well as  $r_g$ ,  $r_c$  and  $r_e$  between them (Neale *et al.* 2003).

#### Assessment of model fit

Model fit was assessed using the likelihood ratio test. A fit statistic that is two times the log-likelihood of the data ( $-2LL$ ) was computed for each model, and compared with  $-2LL$  of saturated models of the means, variances and covariances in the data. The saturated model for the cross-lagged model contained five data groups, one for each of MZ male, MZ female, DZ male, DZ female and DZ opposite-sex twin pairs. Since the bivariate Cholesky decomposition did not include DZ opposite-sex twins, the saturated bivariate

model did not include a calculation group for the DZ opposite-sex twins. The difference in  $-2LL$  between an identified model and a saturated model is  $\chi^2$  distributed, with degrees of freedom (df) equivalent to the difference in the number of parameters estimated, enabling a statistical comparison of fit. Significant  $\chi^2$  results indicate a significant deterioration of fit between models. Model fit was further assessed using Akaike's Information Criterion (AIC), calculated  $\Delta\chi^2 - (2\Delta df)$ . Lower AIC values indicate better-fitting models. Model fit was assessed again when certain parameters were constrained to equal zero to determine their significance. If 'dropping' certain parameters did not produce a significant deterioration of fit, then these parameters were removed from the model.

#### Results

Mean scale scores are presented in Table 1. The phenotypic correlation between full-scale CAST and Conners scores was  $r=0.52$  ( $p<0.001$ ) at both ages. ICCs are presented in Table 2, and suggest genetic influences on each trait at both ages. MZ CTCT ICCs exceed DZ CTCT ICCs at both ages, suggesting genetic influences on their covariation.

#### Cross-lagged model fitting between the ages of 8 and 12 years

Table 3 presents fit statistics for the cross-lagged model and the longitudinal Cholesky decomposition. Equating parameters across sexes led to a significant deterioration of model fit ( $\chi^2_{12}=23.11$ ,  $p<0.05$ ), and hence fit statistics are presented for a cross-lagged model that included quantitative sex differences. It was not possible to drop any longitudinal pathways from the cross-lagged model without significantly reducing the fit of the model, although the fit of the full model was a significant deterioration from the saturated model ( $\chi^2_{174}=539.54$ ,  $p<0.001$ ). This commonly occurs in larger samples, as small differences in trait variance between ages can result in a significant loss of fit. It was not possible to drop any of the longitudinal pathways from the model without reducing its fit (see Table 3). Cross-lagged model parameter estimates are presented in Fig. 2. Both CAST and Conners scores displayed significant developmental stability ( $B_{11 \text{ male}}=0.50$ ,  $B_{11 \text{ female}}=0.47$ ;  $B_{22 \text{ male}}=0.63$ ,  $B_{22 \text{ female}}=0.61$ ). There was a modest, significant, cross-lagged association between CAST at age 8 years and Conners at age 12 years ( $B_{12 \text{ male}}=0.04$ ,  $B_{12 \text{ female}}=0.05$ ). The cross-lagged pathway between Conners at age 8 years and CAST at age 12 years was significant, and stronger ( $B_{21 \text{ male}}=0.14$ ,  $B_{21 \text{ female}}=0.15$ ). These associations

**Table 2.** Intraclass twin correlations, given within each scale within each age (cross-twin correlations), across the two scales within each age (cross-trait cross-twin correlations), and given both within and across each scale across time

	CAST age 8	Conners age 8	CAST age 12	Conners age 12
<b>Monozygotic male twins</b>				
CAST age 8	0.79 (0.77–0.81)	0.31 (0.27–0.35)	0.56 (0.53–0.60)	0.28 (0.23–0.32)
Conners age 8	–	0.84 (0.83–0.85)	0.27 (0.22–0.31)	0.62 (0.58–0.65)
CAST age 12	–	–	0.78 (0.76–0.80)	0.35 (0.31–0.39)
Conners age 12	–	–	–	0.83 (0.82–0.85)
<b>Monozygotic female twins</b>				
CAST age 8	0.78 (0.77–0.80)	0.31 (0.27–0.35)	0.50 (0.47–0.54)	0.25 (0.21–0.30)
Conners age 8	–	0.86 (0.84–0.87)	0.24 (0.20–0.28)	0.66 (0.64–0.69)
CAST age 12	–	–	0.75 (0.74–0.77)	0.30 (0.26–0.34)
Conners age 12	–	–	–	0.86 (0.85–0.87)
<b>Dizygotic male twins</b>				
CAST age 8	0.25 (0.20–0.29)	0.16 (0.11–0.21)	0.15 (0.10–0.20)	0.12 (0.06–0.17)
Conners age 8	–	0.38 (0.34–0.42)	0.15 (0.10–0.20)	0.28 (0.23–0.32)
CAST age 12	–	–	0.27 (0.23–0.32)	0.17 (0.12–0.21)
Conners age 12	–	–	–	0.42 (0.38–0.46)
<b>Dizygotic female twins</b>				
CAST age 8	0.40 (0.36–0.44)	0.19 (0.14–0.23)	0.23 (0.18–0.28)	0.17 (0.12–0.22)
Conners age 8	–	0.44 (0.40–0.47)	0.17 (0.12–0.21)	0.28 (0.24–0.33)
CAST age 12	–	–	0.43 (0.39–0.46)	0.20 (0.16–0.24)
Conners age 12	–	–	–	0.48 (0.44–0.51)
<b>Dizygotic opposite-sex twins</b>				
CAST age 8	0.27 (0.24–0.30)	0.12 (0.09–0.15)	0.18 (0.14–0.21)	0.11 (0.07–0.14)
Conners age 8	–	0.33 (0.30–0.36)	0.10 (0.06–0.14)	0.22 (0.19–0.25)
CAST age 12	–	–	0.28 (0.25–0.31)	0.15 (0.12–0.18)
Conners age 12	–	–	–	0.35 (0.32–0.38)

Data are given as intraclass correlation (95% confidence interval). The correlations are all split by sex and zygosity.

CAST age 8, 31-item Childhood Autism Spectrum Test at age 8 years; Conners age 8, Conners' Parent Rating Scale at age 8 years; CAST age 12, 30-item Childhood Autism Spectrum Test at age 12 years; Conners age 12, Conners' Parent Rating Scale at age 12 years.

held when participants with confirmed or suspected ASD were excluded from the analysis (details available from M.T.).

Further cross-lagged models were fitted to CAST and Conners subscales. The strongest association between the Conners overall scale at age 8 years and the CAST communication subscale at age 12 years was particularly strong ( $B_{\text{male}}=0.18$ ,  $B_{\text{female}}=0.19$ ). Further models revealed no substantial difference in associations with the CAST communication subscale between the Conners hyperactivity/impulsivity ( $B_{\text{male}}=0.22$ ,  $B_{\text{female}}=0.23$ ) and inattention ( $B_{\text{male}}=0.23$ ,  $B_{\text{female}}=0.24$ ) subscales. This association persisted whilst controlling for the effects of general cognitive ability (see Supplementary material).

The cross-lagged model also estimated the proportion of trait variance that was common to both ages. These statistics are presented in the Supplementary material, and suggest that most of the variance in

trait scores at the age of 12 years was unique to that age. These estimates were decomposed into A, C and E influences; while some genetic variation was common to both ages, very little non-shared environmental variance was shared across development. Of the variance in male and female CAST scores at the age of 12 years, 5% was due to non-shared environmental variation at the age of 8 years, while 6% of the variance in Conners scores in males, and 5% in females, was shared with age 8 years.

The fit of the cross-lagged model was compared with the fit of a longitudinal Cholesky decomposition to explore alternative explanations. The AIC value for the longitudinal Cholesky decomposition was lower than that of the cross-lagged model (see Table 3), indicating that this model was a better fit compared with the cross-lagged model. Parameter estimates for this model are presented in Tables 4 and 5.

**Table 3.** Fit statistics for cross-lagged modelling

Model	-2LL <sup>b</sup>	df	Parameters	Comparison with saturated model <sup>a</sup>				Comparison with full cross-lagged model			
				$\Delta\chi^2$ <sup>c</sup>	$\Delta$ df <sup>d</sup>	<i>p</i> <sup>e</sup>	AIC <sup>f</sup>	$\Delta\chi^2$ <sup>c</sup>	$\Delta$ df <sup>d</sup>	<i>p</i> <sup>e</sup>	AIC <sup>f</sup>
Saturated	102184.62	43862	220	–	–	–	–	–	–	–	–
Full model	102724.16	44036	46	539.54	174	<0.001	191.54	–	–	–	–
Cholesky	102529.64	44032	50	345.02	170	<0.001	5.02	–	–	–	–
Drop B <sub>11</sub> <sup>g</sup>	105115.54	44038	44	2930.92	176	<0.001	2578.92	2431.91	2	<0.001	2427.91
Drop B <sub>12</sub> <sup>g</sup>	102926.40	44038	44	741.78	176	<0.001	389.78	242.77	2	<0.001	238.77
Drop B <sub>21</sub> <sup>g</sup>	102718.63	44038	44	534.01	176	<0.001	182.01	34.99	2	<0.001	30.99
Drop B <sub>22</sub> <sup>g</sup>	106805.59	44038	44	4620.97	176	<0.001	4268.97	4121.96	2	<0.001	4117.96

df, Degrees of freedom; AIC, Akaike’s Information Criterion.

<sup>a</sup> The saturated model is a model of the means, variances and covariances in the data.

<sup>b</sup> -2LL is a fit statistic that is minus two times the log-likelihood of the data; this statistic is provided for all models fitted to the data.

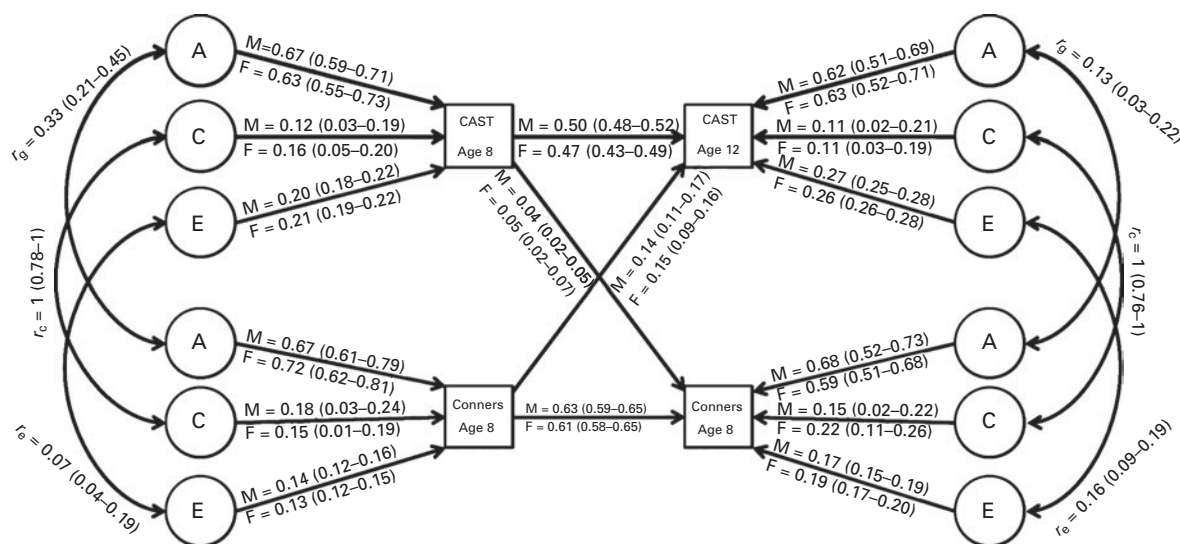
<sup>c</sup>  $\Delta\chi^2$  is the change in -2LL between a given model and the comparison model. The difference in -2LL values is  $\chi^2$  distributed.

<sup>d</sup>  $\Delta$ df is the change in df between a given model and the comparison model, which is equivalent to the difference in the number of parameters between the two models; using  $\Delta$ df and  $\Delta\chi^2$ , it is possible to carry out a statistical comparison of the fit of two models.

<sup>e</sup> Probability statistic derived from the  $\chi^2$  test; significant *p* values indicate a model that is a significantly worse fit compared with the comparison model.

<sup>f</sup> AIC is another fit statistic, which is calculated  $\Delta\chi^2 - (2\Delta$ df). Lower AIC values indicate better-fitting models.

<sup>g</sup> Submodels assessing the significance of stability pathways for traits of autism (B<sub>11</sub>) and traits of ADHD (B<sub>22</sub>), and cross-lagged pathways between autistic traits at the age of 8 years and traits of ADHD at the age of 12 years (B<sub>12</sub>), and traits of ADHD at the age of 8 years and autistic traits at the age of 12 years (B<sub>21</sub>). This is achieved by constraining the selected parameter to equal zero; all submodels are compared with the saturated model and the full cross-lagged model. A significant *p* value indicates that dropping the selected parameter produces a significant deterioration of fit between the submodel and the comparison model.



**Fig. 2.** Cross-lagged model, with parameter estimates. The model suggests a considerable degree of additive genetic influence (A) on each trait individually at both ages, and a modest degree of shared environmental (C) and non-shared environmental (E) influences. Genetic correlations are labelled  $r_g$ , shared environmental correlations are labelled  $r_c$ , while non-shared environmental correlations are labelled  $r_e$ . The arrows leading from CAST age 8 to CAST age 12, and from Conners age 8 to Conners age 12 are stability pathways, while the arrows from each CAST age 8 to Conners age 12 and Conners age 8 to CAST age 12 are cross-lagged pathways that index the influence of each trait on the other. CAST age 8, 31-item Childhood Autism Spectrum Test at age 8 years; CAST age 12, 30-item Childhood Autism Spectrum Test at age 12 years; Conners age 8, Conners’ Parent Rating Scale at age 8 years; Conners age 12, Conners’ Parent Rating Scale at age 12 years; M, male parameter estimate; F, female parameter estimate.



### Bivariate model fitting at 12 years

The best-fitting bivariate Cholesky decomposition was an ACE model with quantitative sex limitation (see Supplementary material for fit statistics). Considerable genetic influences were present for the CAST [ $A_{\text{male}}=0.69$ , 95% confidence interval (CI) 0.61–0.76;  $A_{\text{female}}=0.52$ , 95% CI 0.43–0.61]. Shared environmental influences ( $C_{\text{male}}=0.08$ , 95% CI 0.01–0.15;  $C_{\text{female}}=0.26$ , 95% CI 0.17–0.34) and non-shared environmental influences were modest ( $E_{\text{male}}=0.23$ , 95% CI 0.21–0.26;  $E_{\text{female}}=0.22$ , 95% CI 0.20–0.25). The Conners displayed strong genetic influences ( $A_{\text{male}}=0.76$ , 95% CI 0.67–0.84;  $A_{\text{female}}=0.63$ , 95% CI 0.55–0.71), with modest shared environmental ( $C_{\text{male}}=0.11$ , 95% CI 0.02–0.19;  $C_{\text{female}}=0.21$ , 95% CI 0.13–0.29) and non-shared environmental ( $E_{\text{male}}=0.14$ , 95% CI 0.12–0.15;  $E_{\text{female}}=0.16$ , 95% CI 0.16–0.18) influences in both sexes. The CAST and Conners shared a moderate degree of genetic influences in males ( $r_g=0.41$ , 95% CI 0.34–0.47) and a modest proportion in females ( $r_g=0.23$ , 95% CI 0.15–0.33). Nearly all shared environmental influences were common to CAST and Conners across sexes ( $r_{c\text{ male}}=1$ , 95% CI 0.86–1;  $r_{c\text{ female}}=0.99$ , 95% CI 0.75–1), while non-shared environmental overlap was modest ( $r_{e\text{ male}}=0.16$ , 95% CI 0.10–0.22;  $r_{e\text{ female}}=0.18$ , 95% CI 0.12–0.23). The model was a significantly worse fit to the data than the saturated model ( $\chi^2_{34}=75.76$ ,  $p<0.001$ ).

### Discussion

This study employed genetically informative modelling to explore longitudinal phenotypic associations between traits of ASD and ADHD. While the cross-lagged pathway between traits of ASD at the age of 8 years and traits of ADHD at the age of 12 years was significant, it was weaker than the association between traits of ADHD at the age of 8 years and traits of ASD at the age of 12 years. Such effects occurred above and beyond the association between traits at the age of 8 years. The model demonstrated stability in traits of ASD (Robinson *et al.* 2011; Whitehouse *et al.* 2011) and ADHD (Kuntsi *et al.* 2005; Greven *et al.* 2011) across development. These results suggest that there is a dynamic relationship between traits of ASD and ADHD whereby they influence one another across development. Additionally, our findings are the first to demonstrate that such associations occur above and beyond the concurrent association between these traits at an earlier age.

ADHD is common in individuals with ASD, and traits of ASD appear elevated in ADHD (Clark *et al.* 1999; Reiersen *et al.* 2007). Hence, the strength of the association between earlier traits of ADHD at the age

of 8 years and traits of ASD at the age of 12 years is not entirely surprising; the question is why it is stronger than the reverse association. To gain further insight, cross-lagged modelling was applied to subscales. These models suggested that both ADHD trait subscales at the age of 8 years were most associated with communication difficulties characteristic of ASD at the age of 12 years.

One possibility is that overlap between items on the two measures may have led to this pattern of associations. For example, the CAST communication subscale asks about whether the child is able to keep a two-way conversation going, while the Conners asks whether the child often interrupts others or appears not to hear what is being said to them. However, there is considerable evidence to suggest that the CAST and Conners are valid measures of ASD and ADHD, respectively. For example, Williams *et al.* (2005) reported that the CAST shows high sensitivity and specificity, while Conners *et al.* (1998) found that individuals with a diagnosis of ADHD scored higher than controls on the hyperactivity–impulsivity subscale of the Conners' Parent Rating Scale that the Conners scale in the present study was derived from.

The association between earlier traits of ADHD and later ASD communication traits may indicate language difficulties common to ASD and ADHD. Some of the CAST communication subscale items concern pragmatic language: language use in social communication (Leonard *et al.* 2011) (e.g. 'Is s/he good at turn-taking in conversation?'). Some behaviours associated with ADHD may relate to pragmatic language use; individuals with ADHD may struggle with turn-taking in conversation, while younger children may struggle to sustain attention while playing with other children. Individuals with ADHD have been found to display impairments in pragmatic language not dissimilar to those seen in ASD (Bishop & Baird, 2001). Thus future research may seek to further explore the association between ASD, ADHD and language ability.

Furthermore, the full cross-lagged model suggested different non-shared environmental influences on trait scores at each age. While it is not possible to tease apart genuine non-shared environmental influences from age-specific measurement error (Plomin *et al.* 2008), it is possible that many non-shared environmental influences on traits of ASD and ADHD differ with age. Many changes occur between the ages of 8 and 12 years; for example, children make the transition from elementary to high school, potentially requiring new relationships to be formed and adjustment to a new school environment. Such changes could contribute toward the associations reported here; for instance, a child displaying traits of ADHD

**Table 4.** Standardized parameter estimates for the longitudinal Cholesky decomposition: variance components estimates

	CAST age 8			Conners age 8			CAST age 12			Conners age 12		
	A	C	E	A	C	E	A	C	E	A	C	E
Male <sup>a</sup>	0.69 (0.64–0.70)	0.11 (0.07–0.15)	0.20 (0.18–0.22)	0.70 (0.65–0.75)	0.16 (0.11–0.20)	0.15 (0.13–0.16)	0.65 (0.59–0.70)	0.12 (0.08–0.17)	0.23 (0.21–0.26)	0.74 (0.70–0.79)	0.12 (0.08–0.16)	0.14 (0.12–0.15)
Female <sup>a</sup>	0.64 (0.57–0.70)	0.15 (0.11–0.22)	0.21 (0.19–0.23)	0.69 (0.63–0.74)	0.17 (0.12–0.23)	0.13 (0.12–0.15)	0.57 (0.55–0.66)	0.20 (0.11–0.30)	0.23 (0.21–0.25)	0.67 (0.65–0.73)	0.17 (0.13–0.24)	0.16 (0.15–0.18)

Data are given as estimate (95% confidence interval).

CAST age 8, 31-item Childhood Autism Spectrum Test at age 8 years; Conners age 8, Conners' Parent Rating Scale at age 8 years; CAST age 12, 30-item Childhood Autism Spectrum Test at age 12 years; Conners age 12, Conners' Parent Rating Scale at age 12 years; A, additive genetic influences; C, shared environmental influences; E, non-shared environmental influences.

<sup>a</sup>Separate variance components estimates are provided for males and females.

**Table 5.** Standardized parameter estimates for the longitudinal Cholesky decomposition: aetiological correlations<sup>a</sup>

	Genetic correlations				Shared environmental correlations				Non-shared environmental correlations			
	CAST age 8	Conners age 8	CAST age 12	Conners age 12	CAST age 8	Conners age 8	CAST age 12	Conners age 12	CAST age 8	Conners age 8	CAST age 12	Conners age 12
CAST age 8	–	0.34 (0.30–0.37)	0.66 (0.62–0.71)	0.25 (0.21–0.29)	–	1 (0.92–1)	0.52 (0.29–0.68)	1 (0.81–1)	–	0.07 (0.03–0.11)	0.31 (0.27–0.36)	0.04 (–0.01 to 0.08)
Conners age 8		–	0.33 (0.28–0.38)	0.75 (0.72–0.78)		–	0.73 (0.61–0.90)	0.47 (0.28–0.61)		–	0.08 (0.06–0.12)	0.42 (0.38–0.46)
CAST age 12			–	0.33 (0.29–0.37)			–	1 (0.94–1)			–	0.15 (0.11–0.19)
Conners age 12				–				–				–

Data are given as estimate (95% confidence interval).

CAST age 8, 31-item Childhood Autism Spectrum Test at age 8 years; Conners age 8, Conners' Parent Rating Scale at age 8 years; CAST age 12, 30-item Childhood Autism Spectrum Test at age 12 years; Conners age 12, Conners' Parent Rating Scale at age 12 years.

<sup>a</sup>The aetiological correlations are equated across sexes due to the inclusion of dizygotic opposite-sex twins in the analysis (Neale *et al.* 2006).

upon entering high school may struggle to form new social relationships, and may hence interact less with others. Consideration of specific non-shared environmental influences is possible within the twin design by examining within-pair differences between genetically identical MZ twins (Turkheimer & Waldron, 2000). Such research may shed further light on the cross-lagged associations.

It is important to consider these interpretations of the findings in the context of the relatively poor fit of the cross-lagged model. While deterioration of fit between saturated models and twin models is quite common in large samples (Barrett, 2007), the model was also a poorer fit compared with a longitudinal Cholesky decomposition. Previous research that has employed the cross-lagged model has not included comparison with the longitudinal Cholesky decomposition (e.g. Hallett *et al.* 2010; Greven *et al.* 2011). Such a model was included here as an alternative explanation for the covariance of traits of ASD and ADHD across development. The model suggested that traits of ASD and ADHD at the age of 8 years shared a considerable degree of their genetic influences with the same traits at the age of 12 years. Genetic overlap between traits across development was modest, suggesting that largely different genes may be involved in the covariation of traits of ASD and ADHD between the ages of 8 and 12 years.

We also fitted a bivariate model to data from 12-year-old twins. The model replicated the finding that traits of ASD and ADHD display considerable heritability (e.g. Ronald & Hoekstra, 2011; Asherson & Gurling, 2012). It is noteworthy that shared environmental influences on traits of ASD and ADHD individually were significant in the present study. Twin studies of traits of ASD have often reported models where it is possible to drop shared environmental parameters from the model (e.g. Ronald *et al.* 2006). Similarly for ADHD, many studies suggest that shared environmental influences are negligible. In a large meta-analysis, Nikolas & Burt (2010) reported that shared environmental effects were non-significant. It is hence interesting to note that shared environmental parameters were significant in the present study.

Furthermore, contrary to the findings of an existing study of the same sample at age 8 years (Ronald *et al.* 2008), the bivariate model estimated genetic correlations that differed considerably across sexes. While there was a moderate degree of genetic overlap in males, this was not the case for females, for whom genetic overlap was modest. Although previous twin studies on 12-year-olds did not report such differences (Lichtenstein *et al.* 2010; Lundström *et al.* 2011), these studies did not use sex limitation models. These discrepancies are probably accounted for by our

best-fitting model, which accounted for quantitative sex differences. Hence, these findings suggest that genetic influences on the covariation of traits overlap to a lesser extent in females than in males at the age of 12 years.

The bivariate Cholesky decomposition also estimated significant shared environmental correlations between traits, again in contrast to the earlier study of the same sample at age 8 years (Ronald *et al.* 2008). It is possible that this difference is age-related and further exploration of these associations in adolescent twin samples may prove informative. Indeed, an important direction for future work will be to explore the association between traits of ASD and ADHD in adolescence, an age period which, to date, has been overlooked.

These findings have implications for molecular genetics. The findings from the bivariate and longitudinal Cholesky decomposition add to existing literature suggesting that molecular genetic studies may consider searching for pleiotropic genes underlying ASD and ADHD. Additionally, the cross-lagged model has implications for research on clinical populations. For example, such work may explore whether individuals with ASD and ADHD display similar communication profiles, and whether these contribute toward the co-occurrence of these conditions. A further possibility may be that underlying language and communication difficulties may influence the associations between certain symptoms over time, and hence future work may test this possibility.

This study was not without limitations; due to the large sample, we were unable to employ in-depth clinical assessments. Community-based samples offer the advantage that vast data can be collected, allowing considerable statistical power for twin modelling, while avoiding the referral biases present in clinical samples. It is nevertheless important that these findings are complemented by research with clinically based samples to ensure their clinical relevance.

Cross-lagged parameter estimates were also modest. However, these pathways are partial regression coefficients that account for pre-existing associations. Hence, it is likely a rule, not an exception, that cross-lagged pathways produce conservative estimates (Kenny, 1975), which nevertheless have important scientific implications.

This is the first genetically informative longitudinal analysis of the association between traits of ASD and ADHD. The bivariate model at age 12 years, consistent with prior studies (e.g. Ronald *et al.* 2008), suggests that aetiological influences on traits of ASD and ADHD overlap to an extent. Beyond this, the cross-lagged model suggested that these traits are not static, but influence one another across development. Traits

of ADHD at age 8 years were more predictive of autistic traits at the age of 12 years, particularly communication impairments, than the reverse association. Future research may further explore the association with communication, and the specific aetiological factors driving this association across development.

### Supplementary material

For supplementary material accompanying this paper visit <http://dx.doi.org/10.1017/S003329171200253X>.

### Acknowledgements

The authors thank all the families who participated in the Twins Early Development Study (TEDS). TEDS is funded by a grant from the UK Medical Research Council (no. G0500079). The first author was funded by an Interdisciplinary Doctoral Studentship from the UK Medical Research Council and the Economic and Social Research Council. Research at the Centre for Research in Autism and Education is supported by the Clothworkers' Foundation and Pears Foundation.

### Declaration of Interest

King's College London has received funds for consultancy, invited speaker and/or research grants for work by P.A. from Shire, Lilly, Janssen, Medice and Vifor. F.H. has served as a consultant to Gerson Lehrman Group Healthcare and Biomedical Council and Novartis, and has received honorarium from Novartis for consultancy.

### References

- APA (2000). *Diagnostic and Statistical Manual of Mental Disorders*, 4th edn, revised. American Psychiatric Association: Washington, DC.
- APA (2012). DSM-5 Development: Proposed Revisions, Neurodevelopmental Disorders (<http://www.dsm5.org/proposedrevision/Pages/NeurodevelopmentalDisorders.aspx>). Accessed 19 January 2012.
- Asherson P, Gurling H (2012). Quantitative and molecular genetics of ADHD. *Current Topics in Behavioral Neuroscience* 9, 239–272.
- Barrett P (2007). Structural equation modelling: adjudging model fit. *Personality and Individual Differences* 42, 815–824.
- Bishop DVM, Baird G (2001). Parent and teacher report of pragmatic aspects of communication: use of the Children's Communication Checklist in a clinical setting. *Developmental Medicine and Child Neurology* 43, 809–818.
- Burt SA, McGue M, Krueger RF, Iacono WG (2005). How are parent-child conflict and externalizing symptoms related over time? Results from a genetically-informative cross-lagged study. *Development and Psychopathology* 17, 145–165.
- Clark T, Feehan C, Tinline C, Vostanis P (1999). Autistic symptoms in children with attention deficit-hyperactivity disorder. *European Child and Adolescent Psychiatry* 8, 50–55.
- Conners CK, Sitarenios G, Park JDA, Epstein JN (1998). The revised Conners' Parent Rating Scale (CPRS-R): factor structure, reliability, and criterion validity. *Journal of Abnormal Child Psychology* 26, 257–268.
- de Bruin EI, Ferdinand RF, Meester S, de Nijs PFA, Verheij F (2007). High rates of psychiatric co-morbidity in PDD-NOS. *Journal of Autism and Developmental Disorders* 37, 877–886.
- Goldsmith HH (1991). A zygosity questionnaire for young adults: a research note. *Behavior Genetics* 21, 257–269.
- Greven CU, Asherson P, Rijdsdijk F, Plomin R (2011). A longitudinal twin study on the association between inattentive and hyperactive-impulsive ADHD symptoms. *Journal of Abnormal Child Psychology* 39, 623–632.
- Hall JG (2003). Twinning. *Lancet* 362, 735–743.
- Hallett V, Ronald A, Rijdsdijk F, Happé F (2010). Association of autistic-like and internalizing traits during childhood: a longitudinal twin study. *American Journal of Psychiatry* 167, 809–817.
- Happé F, Ronald A (2008). Fractionable autism triad: a review of evidence from behavioural, genetic, cognitive, and neural research. *Neuropsychology Review* 18, 287–304.
- Happé F, Ronald A, Plomin R (2006). Time to give up on a single explanation for autism. *Nature Neuroscience* 9, 1218–1220.
- Kenny DA (1975). Cross-lagged panel correlation: a test for spuriousness. *Psychological Bulletin* 82, 887–903.
- Kuntsi J, Rijdsdijk F, Ronald A, Asherson P, Plomin R (2005). Genetic influences on the stability of attention-deficit/hyperactivity disorder symptoms from early to middle childhood. *Biological Psychiatry* 57, 647–654.
- Leonard MA, Milich S, Lorch EP (2011). The role of pragmatic language use in mediating the relation between hyperactivity and inattention and social skills problems. *Journal of Speech, Language, and Hearing Research* 54, 567–579.
- Lichtenstein P, Carlström E, Råstam M, Gillberg C, Anckarsäter H (2010). The genetics of autism spectrum disorders and related neuropsychiatric disorders in childhood. *American Journal of Psychiatry* 167, 1357–1363.
- Lundström S, Chang Z, Kerekes N, Gumpert CH, Råstam M, Gillberg C, Lichtenstein P, Anckarsäter H (2011). Autistic-like traits and their association with mental health problems in two nationwide twin cohorts of children and adults. *Psychological Medicine* 41, 2423–2433.
- McLoughlin G, Ronald A, Kuntsi J, Asherson P, Plomin R (2007). Genetic support for the dual nature of attention deficit hyperactivity disorder: substantial genetic overlap between the inattentive and hyperactive-impulsive components. *Journal of Abnormal Child Psychology* 35, 999–1008.
- Mulligan A, Anney RJL, O'Regan M, Chen W, Butler L, Fitzgerald M, Buitelaar J, Steinhausen H, Rothenberger A, Minderaa A, Nijmeijer J, Hoekstra PJ, Oades RD, Roeyers H, Buschgens C, Christiansen H, Franke B, Gabriels I, Hartman C, Kuntsi J, Marco R, Meidad S,

- Mueller U, Psychogiou L, Rommelse N, Thompson M, Uebel H, Banaschewski T, Ebstein R, Eisenberg J, Manor I, Miranda A, Mulas F, Sergeant J, Sonuga-Barke E, Asherson P, Faraone SV, Gill M** (2009). Autism symptoms in attention-deficit/hyperactivity disorder: a familial trait which correlates with conduct, oppositional defiant, and language and motor disorders. *Journal of Autism and Developmental Disorders* **39**, 197–209.
- Neale MC, Boker SM, Xie G, Maes HM** (2003). *Mx: Statistical Modelling*. Virginia Commonwealth University: Richmond, VA.
- Neale MC, Røysamb E, Jacobson K** (2006). Multivariate genetic analysis of sex limitation and G x E interaction. *Twin Research and Human Genetics* **9**, 481–489.
- Nijmeijer J, Hoekstra PJ, Minderaa RB, Buitelaar JK, Altink ME, Buschgens CJM, Fliers EA, Rommelse NNJ, Sergeant JA, Hartman CA** (2009). PDD symptoms in ADHD, an independent familial trait? *Journal of Abnormal Child Psychology* **37**, 443–453.
- Nikolas MA, Burt SA** (2010). Genetic and environmental influences on ADHD symptom dimensions of inattention and hyperactivity: a meta-analysis. *Journal of Abnormal Psychology* **119**, 1–17.
- Oliver BR, Plomin R** (2007). Twins' Early Development Study (TEDS): a multivariate, longitudinal investigation of language, cognition and behavior problems from childhood through adolescence. *Twin Research and Human Genetics* **10**, 96–105.
- Plomin R, DeFries JC, McClearn GE, McGuffin P** (2008). *Behavioral Genetics*. Worth Publishers: New York.
- Price TS, Freeman B, Craig I, Petrill SA, Ebersole L, Plomin R** (2000). Infant zygosity can be assigned by parental report questionnaire data. *Twin Research* **3**, 129–133.
- Reiersen AM, Constantino JN, Grimmer M, Martin NG, Todd RD** (2008). Evidence for shared genetic influences on self-reported ADHD and autistic symptoms in young adult Australian twins. *Twin Research and Human Genetics* **11**, 579–585.
- Reiersen AM, Constantino JN, Volk HE, Todd RD** (2007). Autistic traits in a population-based ADHD twin sample. *Journal of Child Psychiatry and Psychology* **48**, 464–472.
- Robinson EB, Munir K, Munafo MR, Hughes M, McCormick MC, Koenen KC** (2011). Stability of autistic traits in the general population: further evidence for a continuum of impairment. *Journal of the American Academy of Child and Adolescent Psychiatry* **50**, 376–384.
- Ronald A, Edelson LR, Asherson P, Saudino KJ** (2010a). Exploring the relationship between autistic-like traits and ADHD behaviours in early childhood: findings from a community twin study of 2-year-olds. *Journal of Abnormal Child Psychology* **38**, 185–196.
- Ronald A, Happé F, Bolton P, Butcher LM, Price TS, Wheelwright S, Baron-Cohen S, Plomin R** (2006). Genetic heterogeneity between the three components of the autism spectrum: a twin study. *Journal of the American Academy of Child and Adolescent Psychiatry* **45**, 691–699.
- Ronald A, Happé F, Dworzynski K, Bolton P, Plomin R** (2010b). Exploring the relation between prenatal and neonatal complications and later autistic-like features in a representative community sample of twins. *Child Development* **81**, 166–182.
- Ronald A, Hoekstra RA** (2011). Autism spectrum disorders and autistic traits: a decade of new twin studies. *American Journal of Medical Genetics, Part B: Neuropsychiatric Genetics* **156**, 255–274.
- Ronald A, Simonoff E, Kuntsi J, Asherson P, Plomin R** (2008). Evidence for overlapping genetic influences on autistic and ADHD behaviours in a community twin study. *Journal of Child Psychology and Psychiatry* **49**, 535–542.
- Scott FJ, Baron-Cohen S, Bolton P, Brayne C** (2002). The CAST (Childhood Asperger Syndrome Test): preliminary development of a UK screen for mainstream primary-school-age children. *Autism* **6**, 9–31.
- Simonoff E, Pickles A, Charman T, Chandler S, Loucas T, Baird G** (2008). Psychiatric disorders in children with autism spectrum disorders: prevalence, comorbidity, and associated factors in a population-derived sample. *Journal of the American Academy of Child and Adolescent Psychiatry* **47**, 921–929.
- St Pourcain B, Mandy WP, Heron J, Golding J, Davey Smith G, Skuse DH** (2011). Links between co-occurring social-communication and hyperactive-inattentive trait trajectories. *Journal of the American Academy of Child and Adolescent Psychiatry* **50**, 892–902.
- Turkheimer E, Waldron M** (2000). Nonshared environment: a theoretical, methodological, and quantitative review. *Psychological Bulletin* **126**, 78–108.
- Whitehouse AJO, Hickey M, Ronald A** (2011). Are autistic traits in the general population stable across development? *PLoS One* **6**, e23029.
- Williams J, Scott F, Stott C, Allison C, Baron-Cohen S, Brayne C** (2005). The CAST (Childhood Asperger Syndrome Test): test accuracy. *Autism* **9**, 45–68.
- Yoshida Y, Uchiyama T** (2004). The clinical necessity for assessing Attention deficit/hyperactivity disorder (AD/HD) symptoms in children with high-functioning pervasive developmental disorder (PDD). *European Child and Adolescent Psychiatry* **13**, 307–314.