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Why some children with externalising problems develop internalising symptoms: testing two pathways in a genetically sensitive cohort study

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Background: Children with externalising problems are at risk of developing internalising problems as they grow older. The pathways underlying this developmental association remain to be elucidated. We tested two processes that could explain why some children with externalising problems develop internalising symptoms in preadolescence: a mediation model whereby the association between early externalising and later new internalising symptoms is explained by negative experiences; and a genetic model, whereby genes influence both problems. **Methods:** We used data from the Environmental Risk (E-Risk) Study, a 1994–1995 birth cohort of 2,232 twins born in England and Wales. We assessed externalising and internalising problems using combined mothers' and teachers' ratings at age 5 and 12. We measured bullying victimisation, maternal dissatisfaction and academic difficulties between age 7 and 10 and used linear regression analyses to test the effects of these negative experiences on the association between early externalising and later internalising problems. We employed a Cholesky decomposition to examine the genetic influences on the association. **Results:** Children with externalising problems at age 5 showed increased rates of new internalising problems at age 12 ($r = .24$, $p < .001$). Negative experiences accounted for some of the association between early externalising and later internalising problems. Behavioural-genetic analyses indicated that genes influencing early externalising problems also affected later internalising problems. **Conclusions:** Our findings highlight the role of genetic influences in explaining why some children with externalising problems develop internalising symptoms in preadolescence. Negative experiences also contribute to the association, possibly through gene–environment interplay. Mental health professionals should monitor the development of internalising symptoms in young children with externalising problems. **Keywords:** Externalising and internalising problems, failure model, genetic influence, development.

Introduction

Externalising problems such as aggression, rule-breaking and oppositional behaviour are some of the most prevalent disorders in childhood (Ford, Goodman, & Meltzer, 2003). Although most children displaying such behaviour grow up to become well--adjusted adolescents and adults, some will engage in recidivistic, violent criminal activities throughout their life (Moffitt, Caspi, Harrington, & Milne, 2002). Apart from experiencing such persisting antisocial symptoms, children with externalising behaviour are also at risk of developing internalising problems, such as anxiety and depression, both concurrently and as they grow older (Boylan, Georgiades, & Szatmari, 2010; Reef, van Meurs, Verhulst, & van der Ende, 2010). The processes underlying the association between earlier externalising and later new internalising problems are unknown. The aim of the present study was to examine two pathways that could explain why some children with externalising problems develop internalising symptoms during the transition to adolescence.

Mediation model

Children with externalising problems are at risk of experiencing negative situations because of their behaviour: they are victimised by their peers (Van Lier et al., 2012), experience academic difficulties (Masten et al., 2005), and have conflictual relationships with their parents (Burt, McGue, Krueger, & Iacono, 2005). Children who go through such experiences are more likely to develop internalising problems (Arseneault et al., 2006). These findings are consistent with a mediation or 'failure' model (Patterson & Stoolmiller, 1991), whereby negative experiences explain why children with externalising problems develop internalising symptoms as they grow older. Indeed, studies have shown that peer rejection (Kiesner, 2002; Mesman, Bongers, & Koot, 2001) and academic difficulties (Masten et al., 2005) partly mediate the association between early externalising and later internalising problems. However, no study has simultaneously examined negative experiences from a variety of different life contexts, including school, peer relationships and family. One possibility is that it is the cumulation of negative experiences, capturing difficulties in relationships

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with parents and peers, and academic performance, that accounts for the development of internalising symptoms in children with externalising problems.

Genetic influences

The cross-sectional comorbidity between externalising and internalising problems is strongly influenced by genes (Pesenti-Gritti et al., 2008) and the same applies to the stability of both problems (Haberstick, Schmitz, Young, & Hewitt, 2006). It is therefore possible that some of the longitudinal association between early externalising and later internalising problems is also accounted for by genes that influence externalising problems early in life and newly emerging internalising problems in preadolescence. However, there is virtually no research assessing the contribution of genes to the association. In addition, recent research shows strong genetic influences on negative experiences, such as bullying victimisation and conflict with parents (Ball et al., 2008; McAdams, Gregory, & Eley, 2013). This raises the possibility that previous findings on the mediation model partly reflect genetic influences. Examining genetic effects would increase our understanding of the processes underlying the role of negative experiences in the association between early externalising and later internalising problems.

Aims of the present study

The present study aimed to test whether social and academic difficulties, as well as genetic influences, could explain the association between externalising problems in childhood and internalising problems in preadolescence, in a nationally representative sample of twins assessed between the ages of 5 and 12. Negative experiences and genetic influences cannot be thought of as mutually exclusive explanatory processes, thus we expected the association to be mediated by social and academic difficulties, and also influenced by genetic factors. As previous research shows gender differences in externalising and internalising problems (Ford et al., 2003), we tested whether the pathways underlying the association were different for boys and girls. We focused on children's early-onset externalising problems, because these are associated with lifelong difficulties, including social, academic and internalising problems (Moffitt et al., 2002). Moreover, preadolescence is a key period for assessing new internalising problems, which emerge at this time (Ford et al., 2003).

Methods

Sample

Participants were members of the Environmental Risk (E-Risk) Longitudinal Twin Study, which tracks the development of a nationally representative cohort of 2,232 British children. The sample was drawn from a larger birth registry of twins born in England and Wales from 1994 through 1995 (Trouton, Spinath, & Plomin, 2002). Details about the sample have been reported previously (Moffitt & E-Risk Team, 2002). Briefly, the E-Risk sample was constructed from 1999 through 2000, when 1,116 families with same-sex 5-year-old twins (93% of those eligible) participated in home-visit assessments. Families were recruited to represent the UK population of families with newborns in the 1990s, based on residential location throughout England and Wales and mother's age (i.e. older mothers having twins via assisted reproduction were underselected and teenage mothers with twins were over selected). We used this sampling (a) to replace high-risk families who were selectively lost to the register via nonresponse and (b) to ensure sufficient numbers of children growing up in high-risk environments. Follow-up home visits were conducted when the children were aged 7 years (98% participation), 10 years (96%) and 12 years (96%). Children who dropped out from the study were not different on any of the variables analysed in this study compared to children who continued to participate. The sample includes 55% monozygotic (MZ) and 45% dizygotic (DZ) twin pairs. Sex is evenly distributed within zygosity (49% were boys). Parents gave informed consent and children gave assent. Ethical approval was granted by the Joint South London and Maudsley and the Institute of Psychiatry NHS Ethics Committee.

Externalising and internalising problems

We assessed internalising and externalising problems when the twins were aged 5 and 12 using the Child Behavior Checklist for mothers (Achenbach, 1991a) and the Teacher's Report Form (Achenbach, 1991b). Mothers were given the instrument as a face-to-face interview and teachers responded by mail. Both informants rated each item as being 'not true' (0), 'somewhat or sometimes true' (1), or 'very true or often true' (2) in the 6 months before the interview. The externalising problems scale is the sum of the Delinquency and Aggression subscales, including items such as 'gets in many fights,' 'lying or cheating,' and 'screams a lot.' The internal consistencies of mothers' and teachers' reports were .88 and .93 at age 5; and .92 and .96 at age 12. The internalising problems scale is the sum of the Withdrawn and Anxious/depressed subscales, including items such as 'cries a lot,' 'withdrawn,' 'does not get involved with others,' and 'worries'. The internal consistencies of mothers' and teachers' reports were .84 and .85 at age 5; and .88 and .89 at age 12. We combined mothers' and teachers' reports to obtain reliable and comprehensive measures of externalising and internalising problems (Achenbach, Krukowski, Dumenci, & Ivanova, 2005; Arseneault et al., 2003).

Externalising problems ranged from 0 to 97 at age 5 (M = 18.30, SD = 13.69), and 0 to 108 at age 12 (M = 15.65, SD = 14.52) (Table 1). Internalising problems ranged from 0 to 58 at age 5 (M = 12.13, SD = 8.35), and 0 to 72 at age 12 (M = 10.98, SD = 8.30). We observed significantly lower levels of externalising and internalising problems at age 12 compared to age 5 (Table 1). Boys showed higher levels of externalising problems at both ages compared to girls. There were no gender differences in levels of internalising problems.

Mediating variables

We assessed childhood *bullying victimisation* using mothers' reports at age 7 and 10 (Shakoor et al., 2011). We asked mothers whether either twin had been bullied by another child, responding 'never' (0), 'yes' (1) or 'frequently' (2). We averaged mothers' reports at both time points. The test–retest reliability of maternal reports of victimisation was .87 using a sample of 30 parents who were interviewed twice, 3–6 weeks apart.

We assessed *maternal dissatisfaction* with each child using a five minute speech sample (Magana, Goldstein, Karno,

Miklowitz, & Falloon, 1986). Mothers were asked to speak for 5 min about each of their children when they were age 10. Mother's speech samples were audiotaped and coded by two independent trained raters. Maternal dissatisfaction (coded on a 0–5 scale) is a global measure of the whole speech sample, indexing negativism expressed in the interview about the child (Caspi et al., 2004). The inter-rater agreement for maternal dissatisfaction was $r = .90$. The raters were blind to all other E-Risk data.

We assessed *academic difficulties* using teachers' ratings when the children were 7 and 10 years old. Teachers were asked whether children's current mathematical and English performance were: 'far below average' (1), 'somewhat below average' (2), 'average' (3), 'somewhat above average' (4) or 'far above average' (5), compared with pupils of the same age. Scores were averaged across subjects and averaged again across age 7 and 10 to derive a global measure of school performance at primary school.

Statistical analyses

We used linear regression models to examine the effect of the mediating variables on the association between age-5 externalising and age-12 internalising problems (Table 2). The baseline model included externalising problems along with internalising problems at age 5, to control for the effect of earlier internalising problems and predict newly emerging internalising problems at age 12. We then added the mediating variables, first separately and then jointly. We tested whether the reduction in the prediction from age-5 externalising to age-12 internalising problems in the mediation model (i.e. the mediation effect) was significant by using cluster-adjusted bootstrapped standard errors and confidence intervals, with 200 bootstrap replications (Preacher & Hayes, 2008). Participants in this study were pairs of same-sex twins, hence each family contained data for two children, resulting in nonindependent observations. The sandwich or Huber-White variance estimator (Williams, 2000) was used to adjust estimated standard errors to account for the dependence in the data. We used Stata12 for all regression analyses (StataCorp, 2009).

We used twin methodology (Rijsdijk & Sham, 2002) to test the relative influence of genes and the environment on the association between early externalising and later new internalising problems. MZ twins are genetically identical whereas DZ twins share, on average, 50% of their genes. Comparing the correlation of a phenotype within pairs of MZ and DZ twins allows to estimate the relative influence of additive genetic (A), shared environmental (C), and nonshared environmental (E) factors on measures. C represents environmental factors that make members of a family similar, while E represents factors that make members of a family different and includes error of measurement. To estimate the effects of A, C and E on the association between age-5 externalising and age-12 new internalising problems, we fitted a trivariate Cholesky decomposition, illustrated in Figure 1. A_1, C_1 and E_1 represent influences on age-5 internalising problems, which also affect age-5 externalising and age-12 internalising problems via paths a_{21}, c_{21}, e_{21} and a_{31}, c_{31}, e_{31}. A_2, C_2 and E_2 represent influences on age-5 externalising and age-12 internalising problems that are not included in the effects of A_1, C_1 and E_1 already. Paths a_{32}, c_{32} and e_{32} therefore indicate genetic and environmental influences that uniquely explain the association between age-5 externalising and age-12 internalising problems, beyond influences already shared at age 5. A_3, C_3 and E_3 represent remaining influences that are specific to age-12 internalising problems. All variables were log-transformed to reduce their skewness.

Table 1 Externalising and internalising problems in boys and girls at age 5 and 12

	Total		Girls		Boys	
Age	*M (SD)*	*N*	*M (SD)*	*N*	*M (SD)*	*N*
Externalising problems						
5	18.30 (13.69)	2232	15.68 (11.44)	1140	21.05 (15.23)	1092
12	15.65 (14.52)	2142	12.31 (11.60)	1098	19.17 (16.35)	1044
Internalising problems						
5	12.13 (8.35)	2232	12.08 (8.02)	1140	12.19 (8.68)	1092
12	10.98 (8.30)	2141	10.82 (7.81)	1098	11.14 (8.78)	1043

Note: There was a significant difference in problem levels between ages 5 and 12, in externalising [$F(1,1070) = 59.54$, $p < .001$] and internalising problems [$F(1,1070) = 25.12$, $p < .001$]. There was a significant sex difference in externalising problems at age 5 [$F(1,1115) = 57.42$, $p < .001$], and 12 [$F(1,1070) = 77.98$, $p < .001$]. *M* = Mean; *SD* = Standard Deviation, *N* = Number of participants.

Table 2 Associations between age-5 externalising and age-12 new internalising problems, and effects of mediators[a]

	Model 1 B (95% CI)	Model 2 B (95% CI)	Model 3 B (95% CI)	Model 4 B (95% CI)	Model 5 B (95% CI)
Internalising problems age 5	**.28** (.23, .33)	**.27** (.22, .31)	**.28** (.24, .33)	**.27** (.22, .32)	**.26** (.22, .30)
Externalising problems age 5	**.14** (.11, .17)	**.13** (.10, .16)	**.12** (.08, .15)	**.12** (.09, .15)	**.09** (.06, .12)
Peer victimisation	–	**2.38** (1.62, 3.15)	–	–	**2.04** (1.30, 2.79)
Maternal dissatisfaction	–	–	**1.30** (.88, 1.72)	–	**1.21** (.80, 1.62)
Academic difficulties	–	–	–	**1.34** (.92, 1.76)	**1.20** (.79, 1.61)
R^2	.17	.19	.20	.19	.23
Mediator effect B (95% CI)	–	**.01** (.008, .02)	**.02** (.02, .03)	**.02** (.01, .02)	**.05** (.04, .06)

Note: All direct effects and mediation effects (in bold) were significant, $p < .001$.
[a]For better comparison with the results from the behavioural-genetic models, we re-run all regression models using externalising and internalising problems as log-transformed variables. This did not affect the pattern of results. $N_{(Model\ 1)} = 2142$; $N_{(Model\ 2)} = 2127$; $N_{(Model\ 3)} = 2062$; $N_{(Model\ 4)} = 2088$; $N_{(Model\ 5)} = 2031$.

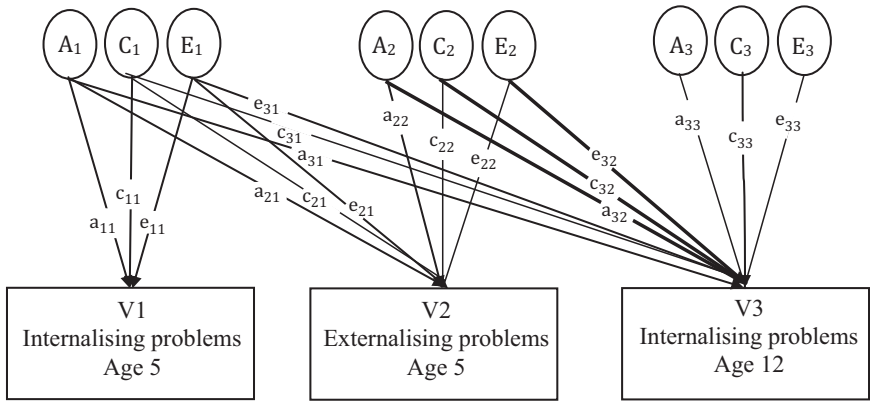

Figure 1 Trivariate Cholesky decomposition. *Note:* A_1, C_1 and E_1 account for variance common to all variables, A_2, C_2 and E_2 account for remaining variance in V2 and V3 not accounted for by A_1, C_1 and E_1; A_3, C_3 and E_3 account for residual variance in V3 only. Bold lines represent the association examined in the present study

Missing data in the genetic analyses were handled using full information maximum likelihood (Baraldi & Enders, 2010). Genetic analyses were conducted using the structural equation modelling program OpenMx (Boker et al., 2011).

Gender differences

We tested for gender differences in the mediation models by including gender and an interaction term between gender and age-5 externalising problems in the regression analyses. In the Cholesky decomposition, we constrained all paths to be equal for girls and boys, and assessed the fit compared to an unconstrained model. All tests for gender differences were nonsignificant, hence we report estimates collapsed across gender.

Results

Are childhood externalising problems associated with preadolescent internalising problems in the E-Risk sample?

Externalising and internalising problems were moderately stable over time, and associated with one another at each time point (Figure 2). Externalising problems at age 5 were associated with internalising problems at age 12, over and above internalising problems at age 5 (r = .24) (Figure 2). Hence, children with high levels of externalising problems at age 5 were at risk of displaying new internalising problems at age 12. In contrast, children with high levels of internalising symptoms at age 5 were not more likely to develop new externalising problems at age 12 (r = −.01).

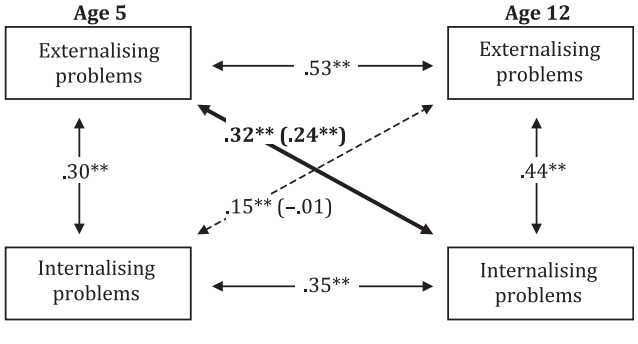

Figure 2 Correlations for externalising and internalising problems cross-sectionally and over time. *Note:* The bold arrow represents the association examined in this study. Correlations in brackets are partial correlations, with age-5 problems controlled for. The sample size varies between N = 2138 and N = 2232, depending on the combination of variables. **p < .001

Can negative experiences mediate the association between early externalising and later internalising problems?

Externalising problems at age 5 were associated with later bullying victimisation (r = .18, p < .001), academic difficulties (r = .24, p < .001) and maternal dissatisfaction (r = .29, p < .001). When we entered the mediators individually into separate regression models, each one of them explained a significant portion of the phenotypic association between age-5 externalising and age-12 internalising problems (7% to 14%; Table 2, Models 2–4). However, in all of these models, externalising problems remained significantly associated with internalising problems at age 12. Entering all mediating variables together resulted in a significant reduction of the effect of externalising problems by 36% (Table 2, Model 5), yet externalising problems remained significantly associated with internalising problems in this model. The mediating variables therefore accounted for some, but not all of the phenotypic association between early externalising and later new internalising problems.

Do genetic influences contribute to the association between early externalising and later internalising problems?

The phenotypic associations between the variables are illustrated in Figure 3. All univariate behavioural-genetic results can be found in the supplementary table S1 (available online). In the Cholesky model,

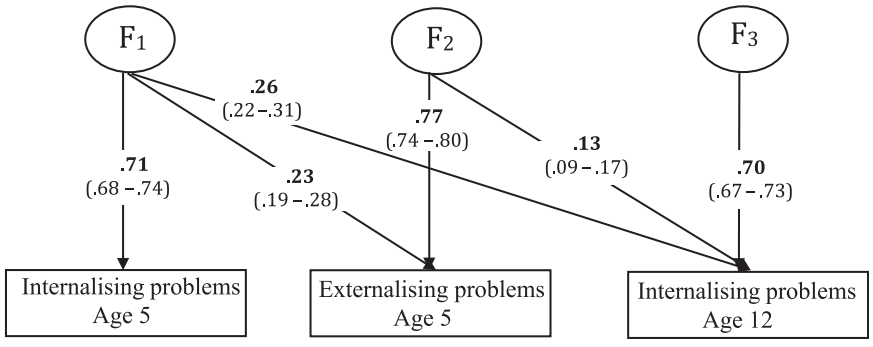

Figure 3 Trivariate Cholesky decomposition of the phenotypic relations among age-5 externalising and age-12 internalising problems. *Note:* F1 represents variance in age-5 internalising problems and covariance with age-5 externalising and age-12 internalising problems; F2 represents variance in age-5 externalising problems and covariance with age-12 internalising problems beyond F1; and F3 represents variance specific to age-12 internalising problems. Estimates are unstandardised (i.e. variances and covariances). To account for the dependence of twin observations, only one twin of each pair was randomly selected into the sample used for the phenotypic Cholesky decomposition, $N = 1116$

the contribution of shared environment (C) was small and nonsignificant; C could be dropped from the model without loss of fit ($\Delta x^2 = 10.31$; $\Delta df = 6$; $p = .11$). In contrast, dropping genetic influences (A) led to a significant deterioration of fit ($\Delta x^2 = 168.63$; $\Delta df = 6$; $p < .001$) (Figure 4). This left genetic (A) and nonshared environmental influences (E) to explain the association between early externalising and later internalising problems. Nonshared environmental influences had significant effects on problems at each age, but there was no overlap between nonshared environmental influences on early externalising and later new internalising problems (Figure 4, path e_{32}). Therefore, nonshared environmental influences could not explain any of their phenotypic covariance. Genes were the only factors left to account for the association. There was a modest but significant overlap between genetic influences on early externalising problems and genetic influences on later new internalising problems (Figure 4, path a_{32}). Dropping this path from the model led to a deterioration of fit ($\Delta x^2 = 30.08$; $\Delta df = 1$; $p < .001$). The results show that 3% of the variance in internalising problems at age 12 was accounted for by genes that also influence externalising problems at age 5. At the phenotypic level, we calculated how much of the association between externalising and internalising problems was accounted for by genetic factors: because the phenotypic covariance is the product of all paths connecting two variables, we multiplied the paths $a_{32} \times a_{22}$ ($\sqrt{.03} \times \sqrt{.58} = .13$). We divided this number by the phenotypic association (.13, Figure 3), which resulted in 1 (interpretable as 100%). This indicates that the association was entirely accounted for by genetic influences. Thus, while the genetic overlap between early externalising and later new internalising problems was relatively small (explaining 3% of the variance in internalising problems at age 12), it accounted for all of the phenotypic covariance between these variables.

Discussion

Children showing externalising problems from an early age are at risk not only of showing persistent antisocial behaviour throughout their lives, but also of developing internalising symptoms as they grow older. We found that the cumulative effect of social and academic difficulties accounted for some of the association between externalising problems in childhood and internalising problems in preadolescence. When examining the influence of genes on the association, our findings show that genetic effects explain why children with externalising problems are at risk of developing internalising problems.

Bullying victimisation, maternal dissatisfaction and academic difficulties partly accounted for the association between early externalising and later internalising problems. These results are in line with findings from other studies using measures of difficulties such as academic problems (Masten et al., 2005) or peer rejection (Kiesner, 2002; Mesman et al., 2001). Our study extends previous work by testing the effect of negative experiences from various settings, which allowed for a comprehensive test of the mediation model. We showed that children with externalising problems are more likely to experience negative situations, and that these experiences are related to their later risk of developing internalising problems. Moreover, each negative experience made an independent and significant, albeit small, contribution, suggesting that each of them mediates slightly different aspects of the association between early externalising and later internalising problems. However, even the cumulative effect of these variables could not explain all of the association, suggesting a role for other influences.

Our study also extends previous research by using a genetically sensitive design and showing that genetic influences explain all of the association between early externalising and later internalising problems. This finding raises implications for the

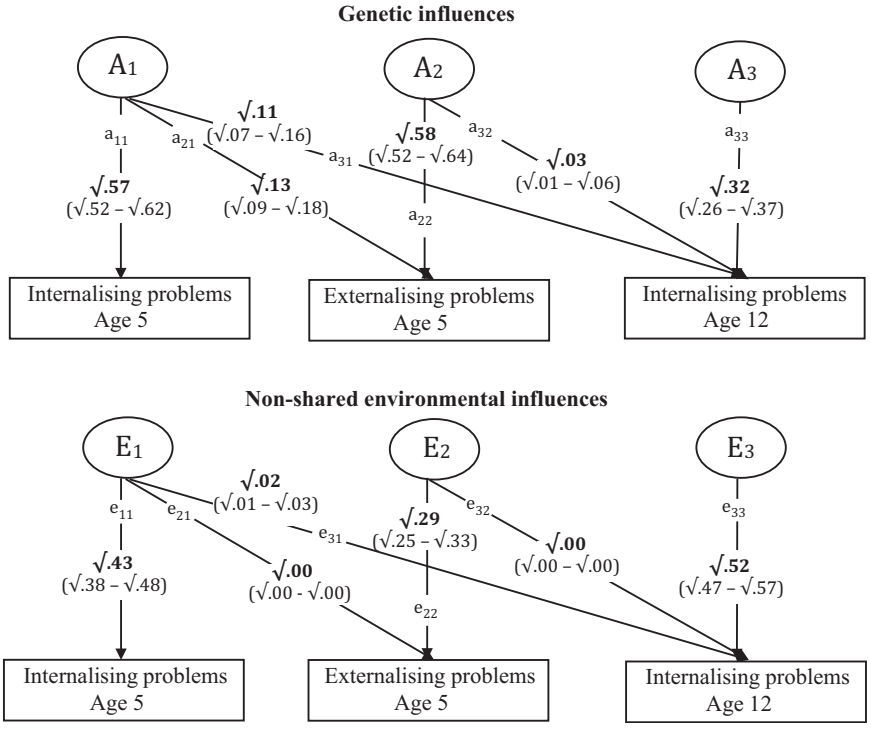

Figure 4 Trivariate Cholesky decomposition partitioning the covariance among age-5 externalising and age-12 internalising problems into genetic (A) and nonshared environmental (E) components. *Note:* Estimates on the diagonal paths indicate how much of the nonshared or genetic influences on one problem also explained variance in other problems. Estimates of genetic and nonshared environment influences on one variable can be obtained by adding the estimates of all paths pointing to this variable (i.e. for the heritability of age-12 internalising problems this would be $A = a_{33} + a_{32} + a_{31}$, = A = .32 + .03 + .11 = .46). *N* = 2232

interpretation of the mediation model discussed above: our results suggest that, between the ages of 5 and 12, negative experiences contribute to the association between early externalising and later internalising problems not through a straightforward environmental pathway. One possibility is that the partial mediation we found is the result of genetic influences common to early externalising and later internalising problems, and negative experiences. This interpretation is consistent with findings of genetic influences on our mediating variables (Ball et al., 2008; McAdams et al., 2013; Walker, Petrill, Spinath, & Plomin, 2004). Genes were also found to influence the associations between externalising problems and negative life experiences (McAdams et al., 2013) and between negative experiences and depressive symptoms (Boardman, Alexander, & Stallings, 2011). In addition, it is plausible that our findings reflect correlations between genes and environments, and interactions between genes and (shared) environments. For example, the association between externalising problems and the mediating variables could be due to evocative gene–environment correlations, whereby a child's genetically influenced externalising problems evokes negative reactions from the environment (McAdams et al., 2013). A gene–environment interaction would occur when negative experiences of a child, such as peer victimisation, interact with genes involved in externalising problems to increase the risk of internalising problems. Variants in the *5*-HTTLPR gene were found to be associated with externalising problems (Hohmann et al., 2009) and, in interaction with bullying victimisation, shown to increase the risk of children's internalising problems in early adolescence (Sugden et al., 2010). These types of gene–environment correlations and interactions are inseparable from purely genetic effects in twin models, because they are contingent on a child's genotype (and hence render MZ twins more similar than DZ twins). Therefore, our findings of strong genetic effects do not negate the presence and the importance of environmental influences. The possibility of gene–environment interplay also implies that modifying the environment of children to reduce their externalising problems could be beneficial in preventing internalising problems. Future research will help to elucidate how genetic vulnerability and environmental influences interact to shape the development of internalising problems in children with externalising problems.

Independent of the nature of the mediation effect, the negative experiences we examined did not account for all of the association between externalising and internalising problems. This is consistent with evidence from previous studies, and suggests a strong role for other, genetically influenced factors in the aetiology of the association. The genetic influences we observed may reflect a broad predisposition to experience symptoms of psychopathology

that manifests itself differently across development. One such predisposition might be irritability, which, as a component of oppositional externalising behaviour, was found to be associated with the development of internalising symptoms in adolescence (Stringaris & Goodman, 2009). Other dispositions are negative emotionality and effortful control: both have been found to be associated with externalising and internalising problems (Eisenberg et al., 2009) and, at least for negative affect, this association seems to be partly genetically mediated (Mikolajewski, Allan, Hart, Lonigan, & Taylor, 2012). Testing the effect of irritability or other dispositions was beyond the scope of this study, but future research should examine the extent to which these contribute to the genetic association between externalising and internalising problems.

Our findings show that some of the genetic influence affecting later internalising problems is already expressed as externalising problems in childhood, but does not manifest itself as internalising problems until preadolescence. The period between childhood and preadolescence is characterised by biological, psychological and social changes (Smetana, Campione-Barr, & Metzger, 2006), and the transition from primary school to the more demanding and autonomous environment of secondary school. It will be interesting to test whether stress associated with these changes interacts with a child's genetic vulnerability for externalising problems in triggering the development of internalising symptoms.

We did not find gender differences in levels of internalising problems at age 12, which is consistent with previous research indicating that it emerges after age 12 (Wade, Cairney, & Pevalin, 2002). As expected, boys showed higher levels of externalising problems compared to girls. However, there was no difference in the association between early externalising and later internalising problems. This indicates that even though girls generally experience lower levels of externalising problems, those with relatively higher problem levels have a similar risk as boys of developing internalising problems. We also did not find any differences between boys and girls in the mediation model or in the magnitude of genetic influences, suggesting that aetiologically similar processes underlie the association between externalising and internalising problems in boys and girls.

Our study has some limitations. First, the observed association between early externalising and later internalising problems could be inflated by using the same informants. However, other studies using different raters have obtained similar results (Kiesner, 2002; Mesman & Koot, 2001). In addition, if the findings were inflated by shared method variance, we would expect to also find an association between early internalising and later new externalising problems, which we did not. However, further studies using different informants, including children themselves, are needed. Second, we chose mediating variables that reflect problems in various life domains, but we cannot exclude the possibility that a different set of variables would have accounted for a larger proportion of the association between externalising and internalising problems. Likewise, we assessed the mediating variables using validated and reliable methods, but it is possible that a different method of measurement, for example using additional items, would have accounted for a greater proportion of the association. Third, our sample comprised twins and we cannot be certain that our results generalise to singletons. However, our findings of an association between early externalising and later internalising problems and the effects of the mediating variables are similar to studies of singletons (Kiesner, 2002; Mesman & Koot, 2001). Fourth, we used global measures of externalising and internalising problems in our study, rather than narrowband dimensions such as delinquency or aggressive behaviour. We would not expect different results when using subtypes, because dimensions within one problem group are highly correlated (Achenbach, Edelbrock, & Howell, 1987; Wadsworth, Hudziak, Heath, & Achenbach, 2001) and the association between externalising and internalising problems does not seem to be restricted to any particular dimensions of these problems (Boylan et al., 2010; Reef et al., 2010). Fifth, given that we used continuous measures, our analyses did not allow us to test whether there is a group of children with externalising problems who are at particularly high risk of developing internalising problems. However, our findings suggest that children with externalising problems who have experienced negative events may have an increased risk. Furthermore, genetically influenced dispositions such as irritability, or a family history of mental health problems, may designate children at high risk for developing internalising problems. Research will help to identify characteristics of children at particularly high risk, to guide clinical screening.

Mental health professionals, teachers and parents should be sensitive to and monitor early symptoms of anxiety and depression among children who show externalising problems from an early age. Reducing externalising problems, as well as preventing children with externalising problems from experiencing social and academic difficulties could decrease their risk of developing internalising problems. Our findings highlight the role of genetic influences in explaining the association. Future research should aim at identifying the pathways through which these influences operate, why they manifest themselves differently across time, and how they interact with children's environments, to identify suitable targets for prevention.

Supporting information

Additional Supporting Information may be found in the online version of this article:

Table S1. Genetic and environmental parameter estimates (and 95% CIs) for externalising and internalising problems at ages 5 and 12.

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Key points

- Children with externalising problems are at risk of developing new internalising problems in preadolescence.
- The association between early externalising and later internalising problems is accounted for by genetic influences.
- Social and academic difficulties account for approximately a third of the phenotypic association; together with the findings of large genetic effects this suggests the possibility that these experiences contribute to the development of internalising problems via gene–environment interplay.
- Mental health professionals, teachers and parents should monitor the development of internalising problems in children with externalising problems.
- Future research will help in understanding the processes by which genetic influences affect the development of internalising problems in children with externalising problems.

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