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Parental Prenatal Symptoms of Depression and Offspring Symptoms of ADHD: A Genetically Informed Intergenerational Study

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Abstract

Objective: The primary aim of the present study was to separate the direct effect of maternal prenatal depression on offspring ADHD from the passive transmission of genetic liability. **Method:** A children-of-twins and siblings design including 17,070 extended-family units participating in the Norwegian Mother and Child Cohort Study was used. Self-ratings were obtained from parents using the Symptom Checklist during pregnancy. Maternal ratings using Conner's Parent Rating Scale were obtained when the children were 5 years of age. **Results:** Genetic influences were important for explaining similarity between parents and offspring. There was also evidence for a maternal effect after accounting for genetic transmission (m = 0.06, 95% confidence interval [CI] = [0.02, 0.09]). **Conclusion:** Our results were consistent with hypotheses suggesting that maternal prenatal depression influences symptoms of ADHD in offspring. However, the effect was weak and a substantial portion of the association could be accounted for by shared genetic influences.*(J. of Att. Dis. XXXX; XX(X) XX-XX)*

Keywords

ADHD symptoms, prenatal depression, children-of-twins, heritability, intergenerational transmission

Introduction

The familiality of lifetime depression is mainly attributable to genetic influences, with heritability estimates ranging from 30% to 40%, whereas environmental influences in common to family members appear comparably negligible (Sullivan et al., 2000). Less is known about genetic contributions to depression occurring at specific periods in life, such as the pregnancy period. Maternal prenatal depression has been found to aggregate within families (Murphy-Eberenz et al., 2006), and a twin study found that genetic influences could account for 37% of the variation (Viktorin et al., 2015).

Maternal prenatal depression has been associated with a range of negative child outcomes (Field, 2011; Glover, 2014; Stein et al., 2014), including symptoms of ADHD (de Bruijn et al., 2009; Luoma et al., 2004; Velders et al., 2011). ADHD and depression have also been found to co-occur within families (Biederman et al., 2008; Faraone & Biederman, 1997). Like depression, ADHD in both childhood and adulthood has been repeatedly shown to be substantially genetically influenced, in studies utilizing both twin designs (Polderman et al., 2015) and molecular genetic methods (Bidwell et al., 2017; Demontis et al., 2019; Pappa et al., 2015). These findings are consistent across studies from different populations (Thapar et al., 2013).

Although an association between maternal prenatal depression and ADHD-related symptoms in the offspring has been found repeatedly, the underlying mechanisms remain poorly understood (Field, 2011; Sciberras et al., 2017). As ADHD is characterized as a neurodevelopmental disorder (American Psychiatric Association, 2013), the early-life environment may potentially be important for its developmental course. A possible explanation for the association is that in utero mechanisms related to prenatal

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depression influence fetal development, later manifesting in ADHD symptoms. Elevated cortisol levels associated with prenatal depression have been suggested as a mediating mechanism leading to adverse child outcomes (Beijers et al., 2014; Field, 2011; Glover, 2014; Stein et al., 2014). However, recent studies have not found consistent associations between prenatal depression and cortisol levels and this mechanism remains debated (Beijers et al., 2014). Other potential mechanisms include, for instance, placental function and blood flow (Sjöström et al., 1997) and epigenetic changes (Oberlander et al., 2008). One way to gain insight into the plausibility of such mechanisms is via the assessment of father–offspring associations (Richmond et al., 2014). Because paternal prenatal depression is unlikely to directly influence the fetus, but may be subject to similar confounding, inclusion of fathers offers a natural negative comparison.

An alternative explanation for the association between maternal prenatal depression and offspring ADHD is that their underlying genetic influences are partially shared. This would induce a phenotypic correlation between mother and offspring attributable to their genetic relatedness. Such an explanation is supported by studies finding genetic correlations between depression and ADHD for both adults (Anttila et al., 2017; Bulik-Sullivan et al., 2015) and adolescents (Cole et al., 2009; Demontis et al., 2019). It is also supported by a sibling comparison study, where it was found that unobserved confounding variables that are shared within the family, rather than a direct effect, were likely to be responsible for the association between maternal prenatal depression and child externalizing problems (Gjerde et al., 2017).

One additional consideration that is often overlooked in studies of intergenerational associations is that of assortative mating, referring to deviations from random mating of partners (Plomin et al., 2013). A recent study found modest correlations among partners for several psychiatric disorders, including depression (Nordsletten et al., 2016). Assortative mating may affect both genetic and environmental resemblance among family members (Rijsdijk & Sham, 2002). Inclusion of both mothers and fathers may, therefore, be important for adequately understanding intergenerational associations.

Our first research question concerns to what extent the association between maternal prenatal depression and offspring ADHD symptoms is consistent with an effect of in utero exposure to depression, versus being attributable to shared genetic influences underlying both traits. Distinguishing between these alternative explanations is important for guiding public health interventions. To our knowledge, no study to date has prospectively investigated genetic overlap between prenatal depression and offspring ADHD symptoms. Our second aim is, therefore, to estimate to what extent prenatal depression and childhood ADHD symptoms share genetic influences. Lastly, we investigate to what extent assortative mating may influence partner similarity in genetic and environmental factors contributing to prenatal depressive symptoms, and account for such influences. We address these questions using an extension of the children-of-twins design (D'onofrio et al., 2003; McAdams et al., 2014, 2018).

Table 1. Number of Parent Sibling Pairs (Individuals in Parenthesis) by Gender and Relatedness.

Gender	MZ	DZ	FS	HS
Mother–mother	88 (157)	51 (96)	5,194 (8,885)	389 (626)
Father–father	26 (47)	16 (32)	3,127 (5,565)	167 (291)
Mother–father		75 (127)	7,475 (13,051)	462 (777)

Note. MZ = monozygotic twins; DZ = dizygotic twins; FS = full siblings; HS = half siblings.

Method

Sample

The study sample comes from the population-based prospective Norwegian Mother and Child Birth Cohort Study (MoBa), recruited between 1999 and 2008 (Magnus et al., 2016). Participants were recruited in connection with a routine ultrasound examination offered to all pregnant women in Norway at Weeks 17 to 18 during pregnancy. The total sample now includes approximately 114,500 children, 95,000 mothers, and 75,000 fathers. Approximately 41% of all invited women participated (Magnus et al., 2016). Version 9 of the quality-assured MoBa data files released in 2015 were used. Written informed consent was obtained from all participants upon recruitment. The MoBa study has been granted a license from the Norwegian Data Inspectorate, and the present study was approved by the Regional Committee for Medical Research Ethics.

The design of the current study was based on comparing members of extended-family units, including pairs of siblings, their partners, and their children (i.e., two related nuclear families). To map the family structure of the MoBa participants, the MoBa cohort was linked with data from Statistics Norway (www.ssb.no). The resulting sample comprised a total of 13,396 children (6,781 boys and 6,615 girls), 26,505 fathers, and 29,407 mothers from 17,070 extended-family units. The relatively high number of parents compared with children results from attrition, but all available data were included in the study. We included parental monozygotic (MZ), dizygotic (DZ), full siblings (FS), and half siblings (HS). In nuclear families with several offspring, one offspring was selected at random. Sample distributions are presented in Table 1.

Table 2. Summary Statistics for Main Variables.

Variable	*M*	*SD*	α
Paternal depression	47.3	8.3	.73
Maternal depression	51.2	10.8	.76
Female ADHD	51.4	9.0	.85
Male ADHD	53.8	10.9	.88

Note. α = Cronbach's alpha; paternal depression = prenatal depression symptoms for fathers; maternal depression = prenatal depression symptoms for mothers; female ADHD = ADHD symptoms for female children; male ADHD = ADHD symptoms for male children.

Classification of Sibling Relationships

Zygosity was determined by genotyping or a questionnaire, which has previously been shown to classify correctly in more than 97% of cases (Magnus et al., 1983). For 16% of the twins, neither genotype or questionnaire data were available. To maximize our sample size, zygosity were predicted for these cases. Predictions were obtained from a logistic regression based on similarity in height, weight, age at menarche, allergies, blood pressure, and metabolism, fitted to the twin pairs with known zygosity. The accuracy of the predictions was estimated to be 87%, based on the training data. Nontwin siblings were classified according to their familial relationship as registered in Statistics Norway.

Measurement of Parental Depression Symptoms

Self-reported depression symptoms covering the last 2 weeks were obtained at Week 30 during pregnancy for mothers and Week 17 for fathers. Symptoms were measured using a short form of the depression dimension of the Symptom Checklist (SCL; Derogatis, 1994) included in the MoBa questionnaire (Tambs & Røysamb, 2014). This version included four items, scored along four ordered categories describing the severity of different symptoms, ranging from *not bothered* to *very bothered*. Items were summed and scaled to *t* scores ($M = 50$, $SD = 10$; see Table 2 for summary statistics). This short-form version of SCL has previously been shown to be highly correlated (.92) with the full SCL depression scale (Tambs & Røysamb, 2014).

Measurement of Child ADHD Symptoms

Symptoms of ADHD were obtained when the children were 5 years of age via maternal reports on the ADHD index of the revised Conner's Parent Rating Scale–Short Form (CPRS-RS; Kumar & Steer, 2003), included in the MoBa questionnaire. The scale consists of 12 items, scored along four ordered categories describing to what extent different symptoms have been a problem for the child during the last month before receiving the questionnaire, ranging from *not true at all* to *very much true*. Items were summed and scaled to *t* scores (see Table 2 for summary statistics).

Statistical Analyses

The statistical method employed was based on previous applications using structural equation models to investigate alternative pathways of intergenerational transmission (McAdams et al., 2014, 2018; Silberg et al., 2010). These models are collectively known as children-of-twin models, because they use differential relatedness among MZ and DZ twin parents and their children to distinguish genetic and environmental modes of transmission (McAdams et al., 2014). In addition to twins, our design included also FS and HS. Under an additive genetic model without assortative mating, the expected genetic correlation is 1 between MZ twins, 1/2 between DZ twins/FS, and 1/4 between HS. The respective correlations are 1/4, 1/8, and 1/16 between their offspring (cousins) and 1/2, 1/4, and 1/8 between offspring and aunt/uncle. These expectations of similarity allows us not only to separate genetic and environmental contributions to variability in parental depressive symptoms and offspring ADHD symptoms but also to separate the passive transmission of genetic influences from parents to offspring from the direct environmental transmission.

A path diagram illustrating key components of the statistical model is shown in Figure 1. All latent variables are modeled as having unit variance so that the square of the regression coefficient equals the variance induced by that variable. Genetic effects on maternal (*M*) and paternal (*F*) prenatal depressive symptoms are represented by latent variables A_m and A_f, with regression coefficient a_p. Similarly, environmental effects are represented by latent variables E_m and E_f, with regression coefficient e_p. There are several alternative processes that may underlie assortative mating (Keller et al., 2010), but they all predict a correlation between the phenotypes of partners. We treat assortative mating as a selection on phenotypes, which have the implications of inducing correlations among both genetic and environmental effects and change the expected genetic correlations among relatives. These implications are represented by the straight line between maternal and paternal phenotypes with covariance parameter d (Neale, 2002).

With respect to offspring ADHD symptoms (O), we allow for the possibility of pleiotropy by distinguishing between genetic effects shared with parental depression (A_o) with coefficient a_o and specific genetic effects (A_o') with coefficient a_o'. This distinction is important to separate genetic from environmental transmission because pleiotropy may create a correlation between offspring genetic effects and the parentally provided environment. Environmental transmission is represented by the regression on the maternal and paternal phenotypes

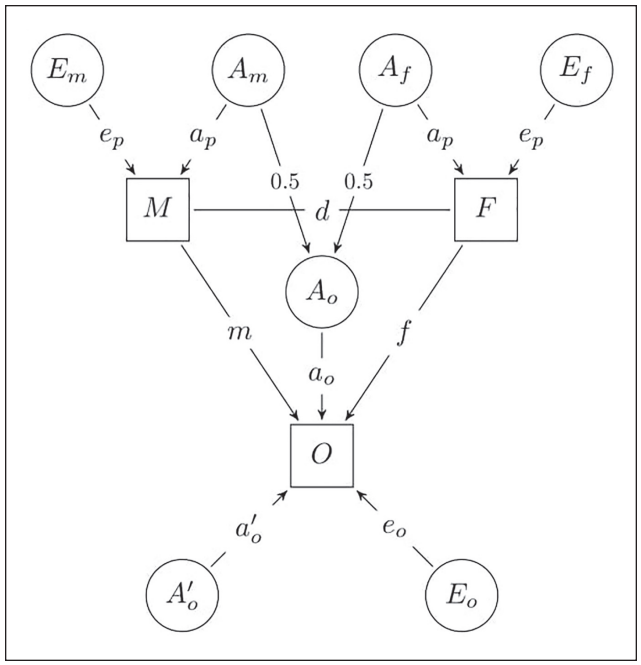

Figure 1. Path diagram of the structural equation model for a nuclear family.

Note. The full diagram would contain a corresponding figure for the family of the other sibling, in addition to two-headed arrows between genetic factors in both families. Observed maternal, paternal, and offspring variables are labeled *M*, *F*, and *O*, respectively. Latent genetic variables are labeled *A* and latent environmental variables are labeled *E*.

with coefficients m and f, respectively. These coefficients can then be interpreted as the effects of parental prenatal depression symptoms, adjusted for common genetic influences between parents and offspring. Lastly, unique environmental effects (E_o) may contribute to offspring ADHD symptoms with coefficient e_o . We allowed for differences in mean and total variance between both adult and offspring males and females (i.e., scalar sex limitation; Neale & Cardon, 2013).

Three alternative models for parent–offspring similarity were compared. In the full model (M1), all parameters were freely estimated, allowing for both passive genetic and direct environmental effects of parents on offspring. In the second model (M2), pleiotropic effects were assumed absent, and only direct environmental effects were assumed from parents to offspring ($a_o = 0$). In the third model (M3), only passive genetic transmission was assumed from parents to offspring ($m = f = 0$). As M2 and M3 are nested under M1, we used likelihood ratio tests to compare the fit of the alternative models in addition to Akaike information criterion (AIC). The models were fitted using OpenMx (Neale et al., 2016). We included all extended-family units with at least one nonmissing response, and assumed that missing data were missing at random.

Results

Descriptive Statistics

The partner correlation in prenatal depression symptoms was .14. The correlation between mothers and offspring ADHD symptoms was .15 and the correlation between fathers and offspring ADHD symptoms was .06. Summary statistics for the main variables are presented in Table 2. Levels of maternal prenatal depression was on average higher than paternal prenatal depression, and more variable. Conversely, male ADHD scores was on average higher and more variable than female ADHD scores. Reliability estimates for all scales were good.

Biometrical Analyses

Model comparisons indicated that parent–offspring similarity could not be adequately explained by direct environmental effects alone ($\chi^2(1) = 15.04$, $p < .001$), or passive genetic effects alone ($\chi^2(2) = 67.07$, $p < .001$). The full model was also favored by AIC. We therefore proceeded by interpreting results from the full model. Parameter estimates and fit statistics for all three models are presented in Table 3.

Our first aim was to estimate the direct environmental effects of maternal and paternal prenatal depression symptoms on child ADHD symptoms, after accounting for shared genetic influences. The maternal effect associated with prenatal depression was positive ($m = 0.06$, 95% confidence interval [CI] = [0.02, 0.09]), whereas the paternal effect was weaker and in the opposite direction ($f = -0.04$, 95% CI = [−0.08, 0.00]). The corresponding standardized effects were 0.07 and −0.05, respectively.

Our second aim was to investigate the relative contributions of genetic and environmental influences on both parental prenatal depression symptoms and child ADHD symptoms. Genetic effects accounted for 17% of variability in prenatal depression symptoms. For offspring ADHD symptoms, genetic effects shared with parental prenatal depression accounted for 17% of variability, whereas specific genetic effects accounted for another 42%. This corresponds to a genetic correlation of .54 between prenatal depression and offspring ADHD symptoms.

Lastly, we investigated the effects of assortative mating on the correlation among partners in genetic end environmental effects contributing to prenatal depression symptoms. The phenotypic correlation among partners was estimated to .15. Considering this modest correlation and relatively low impact from genetic influences on prenatal depression, the expected genetic correlation among partners is only .02, the environmental correlation is .12, and the correlation between genetic and environmental effects is .05.

Table 3. Results From the Fitted Models.

	M1			M2			M3		
Parameter	Est	Est^s	*SE*	Est	Est^s	*SE*	Est	Est^s	*SE*
m	0.06	0.07	0.02	0.13	0.15	0.01	0	0	—
f	−0.04	−0.05	0.02	0.03	0.04	0.01	0	0	—
a_p	4.41	0.41	0.23	4.42	0.41	0.24	4.41	0.41	0.23
a_o	3.74	0.42	1.13	0	0	—	4.12	0.46	0.33
e_p	9.84	0.91	0.11	9.83	0.91	0.11	9.83	0.91	0.11
e_o	5.69	0.63	1.31	5.88	0.66	1.11	5.58	0.62	0.61
a_o'	5.79	0.64	1.69	6.62	0.74	0.99	5.69	0.63	0.61
d	17.00	0.15	0.80	17.00	0.15	0.77	16.99	0.15	0.76
Log-likelihood		−254,577.4			−254,584.9			−254,610.9	
AIC		509,182.8			509,195.8			509,245.9	

Note. M1 = model with both genetic and environmental transmission; M2 = model with only environmental transmission; M3 = model with only genetic transmission; Est = estimate; *SE* = standard error of estimate on original scale; Est^s = standardized estimate; m = maternal effect of prenatal depression; f = paternal effect of prenatal depression; a_p = additive genetic effect on parental prenatal depression; a_o = additive genetic effect on child ADHD symptoms shared with parental prenatal depression; e_p = unique environmental effect on parental prenatal depression; e_o = unique environmental effect on child ADHD symptoms; a_o' = additive genetic effect specific to child ADHD symptoms; d = covariance between partners in prenatal depression; AIC = Akaike information criterion.

In the supplemental material, we present a sensitivity analysis after removing twins from the sample. The results were not sensitive to this exclusion.

Discussion

In the current study, we used a children-of-twins and siblings design, allowing the association between parental prenatal depression and offspring ADHD to be decomposed into passive genetic transmission and direct environmental effects. Our analyses revealed three main results. First, we found a significant association between maternal prenatal depression and ADHD symptoms in the offspring that was not attributable to shared genetic influences. Second, we found evidence for genetic influences on both parental prenatal depression and child ADHD and partially shared genetic influences. Lastly, we found a modest correlation in prenatal depression symptoms between partners, which does not appear to be important for the distribution of offspring ADHD symptoms.

The current study has several strengths. First, the MoBa study is a prospective study, which is critical for studying long-term effects. Retrospective assessments would make it very difficult to accurately separate prenatal depression from pregestational and postnatal depression, which would make the results less interpretable. Second, we used a large population-based sample. After selection into MoBa, the only criterion for inclusion in the analysis was having a sibling also participating in the MoBa study. This is likely to increase the generalizability of our findings, compared with more targeted twin studies. Third, due to the complexity of intrafamilial interactions, it appears difficult to justify studies of mother–child associations a priori, without considering the role of fathers and shared genetic influences. Our findings should also be interpreted with respect to limitations in our study design. First, a potential weakness in our analyses is that we did not account for the possibility of unmeasured environmental influences shared between members in the nuclear family. For example, low socioeconomic status is often found to be associated with higher levels of psychiatric morbidity, including adulthood depression (Lorant et al., 2003) and childhood ADHD (Russell et al., 2016). Such effects could distort estimates of both genetic and environmental parent–offspring associations. However, because current knowledge of the domain is relatively sparse, it would be difficult to select the relevant variables and meaningfully model their effects on parent–offspring similarity. We emphasize that our results should not be understood to mean that maternal depression causes ADHD, but rather that within the broad explanations considered, separating genetic from environmental transmission, our results are consistent with both. It will be up to future investigations to address other alternative explanations. Second, measurements of maternal prenatal depression and offspring ADHD were both obtained via maternal reports. If mothers with higher levels of prenatal depression also rate their children higher for reasons unrelated to their actual levels of ADHD, this is a source of confounding that could explain why the effect of maternal prenatal depression was larger than of paternal prenatal depression, which was assessed via fathers' self-reports (Boyle & Pickles, 1997). Third, because maternal and paternal prenatal depression was not assessed at the same gestational age, the validity of interpreting paternal depression as a negative control condition may have been compromised

and the similarity among parents underestimated. Fourth, assessment of maternal depression was restricted to the third trimester and our results may not generalize to other periods of the pregnancy or to the pregnancy as a whole. Fifth, although our findings are consistent with an environmental effect of maternal prenatal depression on child ADHD symptoms, prenatal depression often co-occurs with other behaviors, such as stress and nicotine and alcohol use (Field, 2011), that have also been found to be risk factors for ADHD (Eilertsen et al., 2017; Thapar et al., 2013). Further knowledge regarding the role of maternal prenatal depression is likely gained by using designs that permit such factors to be held constant. Sixth, it has been suggested that prenatal effects may be sex specific (Beijers et al., 2014), and that ADHD risk may manifest more similar to depression in females than in males (Martin et al., 2018). Unfortunately, we did not have sufficient statistical power to investigate sex-specific patterns of intergenerational transmission (McAdams et al., 2018). Last, it should be noted that the study is based on a Norwegian cohort and demographic variables may differ from other populations due to selection and attrition. Compared with the complete Norwegian birth population, several exposure–outcome associations have been found to be similar (Nilsen et al., 2009). We have previously discussed potential impacts of attrition (McAdams et al., 2019).

The first aim of this study was to investigate whether the association between maternal prenatal depression and offspring ADHD symptoms was consistent with an environmental effect of exposure during pregnancy. To do this, we jointly modeled shared genetic influences underlying both behaviors and separated maternal from paternal effects, which is assumed to have no mechanism by which to directly affect the developing fetus. There are several theoretical models for potential pathways between maternal prenatal depression and ADHD in the offspring (Field, 2011). Fetal programming hypotheses postulate that in utero exposure alters fetal development, which later manifests in negative outcomes. Elevated cortisol levels and changes in uterine blood flow accompanying depression have been suggested as possible mechanisms that affect the offspring's brain development (Beijers et al., 2014; Field, 2011; Glover, 2014; Stein et al., 2014). Our analysis indicated that, after controlling for shared genetic influences, there was a maternal effect of prenatal depression on offspring ADHD symptoms that was larger than the paternal effect. These findings are consistent with a small environmental effect of maternal depression on offspring ADHD symptoms. Our analysis also indicated a small paternal effect, in the opposite direction. Because we are unaware of any theoretical models suggesting effects of paternal prenatal depression, we avoid further interpretations of this association, noting that the interpretation of paternal depression as a negative control may be compromised (Brew et al., 2017). Although these findings are consistent with hypotheses of fetal programming, there are several alternative interpretations. For example, treatment of depression via antidepressants may explain the association between maternal depression and offspring ADHD, but previous studies have not found a link between prenatal use of selective serotonin receptor inhibitors and symptoms of ADHD, unlike other developmental problems (Brandlistuen et al., 2015; Lupattelli et al., 2018). Another alternative interpretation is that prenatal depression co-occurs with later depression, which has also been associated with child behavior problems (Gjerde et al., 2017). There are also other pathways through which maternal depression could influence offspring development, such as reduced responsiveness toward the child (Pearson et al., 2012) or epigenetic changes (Beijers et al., 2014; Field, 2011; Glover, 2014; Stein et al., 2014). The current study was not designed for evaluating such alternative mechanisms. Future studies could, for example, study methylation patterns in siblings discordant for exposure to prenatal maternal depression.

A prerequisite for studying intergenerational transmission of genetic influences is that both the parental and child behaviors are under genetic influence. We found that genetic influences accounted for 17% of variation in parental prenatal depression. These estimates are lower than what is typically found in twin studies of lifetime major depression (Kendler et al., 2001; Sullivan et al., 2000) as well as a study considering depression during the whole pregnancy period, finding genetic influences to account for 37% of variation (Viktorin et al., 2015). Our estimates are closer to findings from studies using family-based designs to study depression symptoms over shorter time intervals (Czajkowski et al., 2010; Silberg et al., 2010). It appears plausible that assessments covering narrower time intervals will be more susceptible to recent environmental circumstances, and consequently show lower heritability than assessments covering longer time intervals. It has also been suggested that prenatal depression may be distinctive in kind from depression in general, as genetic influences have been shown to be only partially overlapping (Viktorin et al., 2015). Currently, little is known about the genetic etiology of prenatal depression, and more research is needed to understand whether there are distinctive mechanisms causing variation at this particular period.

For child ADHD symptoms, genetic influences accounted for 59% of the total variation. This is comparable with other estimates at similar ages (Eilertsen et al., 2019; Kuntsi et al., 2005; Rietveld et al., 2004). This adds further support to the well-replicated finding of substantial genetic influences on childhood ADHD.

Our results also suggested partially common genetic influences for prenatal depression and child ADHD. Designs using twins and their children to assess the importance of genetic and environmental influences underlying

parent–offspring similarity have been used to investigate a variety of research questions (McAdams et al., 2014). In a study of parental depression and adolescent offspring externalizing problems, no shared genetic influences were found (McAdams et al., 2015). In another genetically informative study, the association between maternal prenatal stress and ADHD symptoms in children aged 4 to 10 years was found to be accounted for by genetic factors (Rice et al., 2010). The reasons for these mixed findings are unclear, but highlight the complex etiology of parent–offspring associations. Developmentally emerging genetic influences have been indicated for both ADHD (Chang et al., 2013) and depression symptoms (Scourfield et al., 2003), and the extent to which these are overlapping may, therefore, differ throughout the life span.

A recent study found indications of assortative mating across a range of psychiatric disorders. Averaged across the gender of the proband, the correlation of major depression between partners was estimated at .16 (Nordsletten et al., 2016). Silberg et al. (2010) found correlations of .17 and .20 for depressive symptoms. These estimates are close to our estimate of .14. We further modeled assortative mating as a selection of similar phenotypes, inducing correlations in both genetic and environmental factors between partners. Because the partner correlation and heritability of prenatal depression were both modest, assortment does not appear to be important for understanding the association between maternal prenatal depression and offspring ADHD symptoms. However, the current study was not designed to investigate alternative models of partner similarity, and there may be several mechanisms underlying partner resemblance such as convergence over time or social homogamy (Keller et al., 2010).

Our analyses indicated that shared genetic influences are important for understanding why maternal depression and offspring ADHD symptoms co-occur within families, but cannot fully account for this association. Evaluated together with the weaker effect of paternal prenatal depression, we could not discard a hypothesis suggesting that maternal prenatal depression influences fetal development, which later manifests in ADHD symptoms. Carefully designed studies that can separate other alternative processes underlying the association between maternal prenatal depression and offspring ADHD are needed.

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Supplemental Material

Supplemental material for this article is available online.

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