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Intergenerational transmission of ADHD behaviors: genetic and environmental pathways

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Abstract

Background. We investigate if covariation between parental and child attention-deficit hyperactivity disorder (ADHD) behaviors can be explained by environmental and/or genetic transmission.

Methods. We employed a large children-of-twins-and-siblings sample ($N = 22\,276$ parents and 11 566 8-year-old children) of the Norwegian Mother, Father and Child Cohort Study. This enabled us to disentangle intergenerational influences via parental genes and parental behaviors (i.e. genetic and environmental transmission, respectively). Fathers reported on their own symptoms and mothers on their own and their child's symptoms.

Results. Child ADHD behaviors correlated with their mother's (0.24) and father's (0.10) ADHD behaviors. These correlations were largely due to additive genetic transmission. Variation in children's ADHD behaviors was explained by genetic factors active in both generations (11%) and genetic factors specific to the children (46%), giving a total heritability of 57%. There were small effects of parental ADHD behaviors (2% environmental transmission) and gene–environment correlation (3%). The remaining variability in ADHD behaviors was due to individual-specific environmental factors.

Conclusions. The intergenerational resemblance of ADHD behaviors is primarily due to genetic transmission, with little evidence for parental ADHD behaviors causing children's ADHD behaviors. This contradicts theories proposing environmental explanations of intergenerational transmission of ADHD, such as parenting theories or psychological life-history theory.

Original Article

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Abbreviations:
ACE: additive genetics, shared environment, and environment; ADHD: attention-deficit hyperactivity disorder; MoBa: Norwegian Mother, Father and Child Cohort Study; RS-DBD: Rating Scale for Disruptive Behaviour Disorders

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Attention-deficit hyperactivity disorder (ADHD) is defined as a neurodevelopmental condition diagnosed behaviorally based on age-inappropriate inattention, hyperactivity, and impulsivity that interferes with functioning (American Psychiatric Association, 2013).

Children with ADHD-like traits often have parents with ADHD-like traits (De Zeeuw et al., 2020; Tung, Brammer, Li, & Lee, 2015). This resemblance could be due to environmental transmission through parental behaviors, genetic inheritance, gene–environment correlation, environmental exposures that influence both parents and children, or a combination of such processes. Understanding the relative importance of these mechanisms is key for progress in ADHD science (Sonuga-Barke et al., 2023). It is possible that intergenerational transmission of ADHD behaviors are entirely driven by genes transmitted from parent to child, given that ADHD is estimated to be highly heritable ($h^2 \approx 70$–80%) (Brikell, Kuja-Halkola, & Larsson, 2015; Franke et al., 2012; Nikolas & Burt, 2010). However, these heritability estimates are based on the classical twin design, which assumes that genetic and environmental components are uncorrelated. Using data from extended families (including twins) allows for a detailed composing of sources of intergenerational transmission, including gene–environment correlation. Extended family data allow for the separation of passive genetic effects (e.g. inheritance of ADHD-associated genes) from direct environmental effects (e.g. effect of growing up with parents portraying ADHD behaviors). Extended family data also allow for estimation of

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whether ADHD behaviors in children and adults have different genetic risk profiles because the ADHD phenotype might change over time.

Investigating ADHD with different designs, such as the extended family design and molecular genetic designs, is important because every method has different strengths and weaknesses that can bias genetic or environmental estimates downward or upward (D'Onofrio et al., 2003; McAdams et al., 2018; Neale & Maes, 2004). Using parental polygenic scores for ADHD – a summary of individuals' genetic liability to ADHD based on the effects of many genetic variants – De Zeeuw et al. (2020) and Pingault et al. (2023) found no evidence that the parents affected their children's ADHD behaviors beyond the genetic transmission. Although compelling, these studies could not fully rule out environmental transmission because polygenic scores only account for a very small proportion of the genetic variance in ADHD (Demontis et al., 2019), meaning that the complete effects from the non-transmitted alleles have not been measured.

Some studies have made a case for environmental transmission of ADHD behaviors, showing that parents with ADHD are more likely to be both harsh and lax parents (Park, Hudec, & Johnston, 2017). Similarly, Tung et al. (2015) used longitudinal data to show that harsh parenting behaviors were associated with ADHD behaviors in both parents and children. Reasons for expecting environmental transmission of psychological traits include imitation of parental behaviors, but also more complex explanations. The psychological 'life-history theory' attempts to explain how traits may develop in response to childhood experiences (Nettle & Frankenhuis, 2020). This evolutionary theory has been used to explain the development of ADHD behaviors (Del Giudice, 2014; Frederick, 2012), although it has also been theoretically challenged (Berg, Kuja-Halkola, D'Onofrio, Lichtenstein, & Latvala, 2021; Sheppard & Van Winkle, 2020; Zietsch & Sidari, 2020). In this framework, ADHD behaviors are expected to reflect a 'fast' life-history strategy, which emphasizes short-term fitness gains (impulsivity and future discounting) rather than potential long-term fitness gains (planning for the future). This approach prescribes an important role for parental behavior in the intergenerational transmission of traits (Belsky, Steinberg, & Draper, 1991; Del Giudice, 2014; Frederick, 2012). Some studies indicate that ADHD behaviors may develop in response to environmental stressors, such as family poverty (Larsson, Sariaslan, Långström, D'Onofrio, & Lichtenstein, 2014; Miller et al., 2018) or low education (Torvik et al., 2020). Although these studies indicate a role of the family in the development of ADHD, the role of parental ADHD behaviors specifically remains unknown.

Kinship-based genetic designs, such as this one, provide an alternative to molecular genetic designs. Although kinship-based studies do not identify specific alleles, all genetic variation is modeled.

The present study

Using a large sample and an extended children-of-twins-and-siblings design, we investigate the degree to which covariation between parental and child ADHD behaviors can be explained by environmental *v.* genetic transmission. We study whether parental ADHD behavior is an environmental factor that affects child ADHD beyond genetic factors shared between parents and children (Hart, Little, & Van Bergen, 2021). This is crucial given that parents provide their children with both their home environment and their genes. If children's levels of impulsivity, hyperactivity, and inattention are influenced by parental ADHD behaviors, parental ADHD behaviors should account for child ADHD behaviors above and beyond the inherited genetic influence. Measured ADHD behaviors in the extended families of twins and siblings allow for the separation of 'direct environmental effects' (F) of growing up with parents with ADHD behaviors from the 'passive genetic effects' (A) due to inheritance (McAdams et al., 2014). We also model other environmental influences shared between siblings, such as neighborhood and school effects (C'), and genetic variance specific to childhood (A').

Methods

Sample

The sample comes from the Norwegian Mother, Father, and Child Cohort study (MoBa) (Magnus et al., 2016). MoBa is a population-based pregnancy cohort study conducted by the Norwegian Institute of Public Health. Participants were recruited from all over Norway from 1999 to 2008. Mothers to be consented to participate in 41% of the pregnancies. The cohort now includes 114 500 children, 95 200 mothers, and 75 200 fathers. The MoBa sample primarily includes individuals with a Norwegian/European ancestry. The current study is based on version 11 of the quality-assured data files released for research in 2018. The establishment of MoBa and initial data collection was based on a license from the Norwegian Data Protection Agency and approval from The Regional Committees for Medical and Health Research Ethics. The MoBa cohort is now based on regulations related to the Norwegian Health Registry Act.

Within MoBa, we included extended family units composed of two nuclear families where one parent in each nuclear family is a sibling to one parent in the other family. In the child generation we included up to two children per nuclear family. For nuclear families with more than two children, two were selected at random. A complete unit therefore included eight individuals: two mothers, two fathers, and up to four children.

The selection procedure resulted in response data from 22 276 parents and 11 566 children. The parental generation included 69 pairs of monozygotic twins (39 with complete data; 27 pairs where both are mothers, 12 fathers), 95 pairs of dizygotic twins (24 complete; 6 mothers, 4 fathers, 14 opposite-sex), 9442 pairs of full siblings (2814 complete; 827 mothers, 651 fathers, 1336 opposite-sex), and 714 pairs of half siblings (182 complete; 68 mothers, 29 fathers, 85 opposite-sex). Of the 22 276 parents, 11 143 were partners, and 11 133 were siblings. The offspring generation included 1445 pairs of full siblings.

The relatively low number of siblings in the offspring generation has two reasons. First, fewer couples have participated in MoBa after the first pregnancy. Second, measures of ADHD behaviors for children were obtained 3 years later than for parents, with a lower participation rate (Magnus et al., 2016).

Measures

Measures of maternal and paternal ADHD behaviors were obtained from a six-item screener of the Adult ADHD Self-Report Scale (Kessler et al., 2005). Mothers reported on their own ADHD behaviors when their children were approximately 3 years old, whereas fathers did so during the pregnancy. Measures of children's ADHD behaviors were obtained from maternal responses to 18 items from the Rating Scale for

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Disruptive Behaviour Disorders (RS-DBD; Silva et al., 2005) when the children were approximately 8 years old. At this point, the mothers had a mean age of 38.68 (S.D. = 4.69) and fathers 41.26 (S.D. = 5.4). The RS-DBD can be subdivided into inattention and hyperactivity-impulsivity traits.

Individuals missing more than 50% of items were excluded from the analysis. For the remaining individuals, their values were imputed by the mean for that person. For childhood ADHD behaviors, we computed both aggregate scores and a separate score for the inattention and hyperactivity sub-scales. Missing response data and varying family compositions were modeled using full information maximum-likelihood. This allowed us to include data across varying family compositions (e.g. parents with less than two children) and missing patterns (e.g. missing data from one individual in a twin pair).

For the adult scale, the estimated reliability was $\alpha = 0.70$. For the child scales, the estimated reliabilities were $\alpha = 0.91$ for the aggregate scale, and $\alpha = 0.87$ and $\alpha = 0.85$ for the inattention and hyperactivity subscales, respectively.

Statistical analysis

Our modeling approach to intergenerational transmission of ADHD behaviors is based on that used by Silberg, Maes, and Eaves (2010). The children-of-twins-and-siblings model is an extension of the classical ACE model for twin designs in which the phenotype is decomposed into an additive genetic component (A), a shared environmental component (C), and a unique environmental component (E) (D'Onofrio et al., 2003; McAdams et al., 2014; Neale & Maes, 2004). In addition to pairs of twins, children-of-twins-and-siblings models extend this design by including partners and children of the twins. This allows us to compare alternative models of intergenerational transmission. We can illustrate the logic of the model by considering a mother who has an identical twin sister. Her children will be as genetically related to their mother as to their aunt. If the children's ADHD behaviors are equally correlated with their mother's as with their aunt's, it suggests that the correlation is fully due to shared genes. On the other hand, if the children correlate more with their mother, it suggests that the environment the mother provides has an effect as well (Hart et al., 2021).

The path diagram in Fig. 1 shows the essential features of the model. Measured maternal, paternal, and offspring ADHD behaviors from mothers, fathers, and children are depicted by rectangles labeled *M*, *P*, and *O*, respectively. Latent variables are depicted by circles and observed variables by rectangles. We describe parental ADHD behaviors as a function of additive genetic effects (*A*), environmental effects shared by siblings (*C*), and environmental effects unique to the individual, including measurement error (*E*). The strength of these influences is indicated by the path coefficients depicted by the arrows in the figure. We model similarity in ADHD behaviors between partners as phenotypic assortment, meaning that we assume that partners have selected each other based on their expressed levels of ADHD behaviors. These implications are represented with the horizontal line (i.e. co-path) labeled *d* between maternal and paternal ADHD behaviors. The parents that were half siblings are modeled with the same amount of environment shared as full siblings. Half siblings might be less likely to cohabitate than full siblings, but we do not know by how much and hence do not model the shared environmental correlation at an arbitrarily different point.

With respect to the offspring generation, we split the additive genetic effects into two components, one shared with parental ADHD behaviors (*A*) and one unique to offspring ADHD behaviors (A', pronounced as *A* prime). This allows us to determine whether genetic effects are different across the two generations. This is important because genetic influences on ADHD behaviors might partly depend on age (Eilertsen et al., 2018).

The environmental family effects on offspring were split into one component directly attributable to parental ADHD behaviors (*F*) and one component due to other shared environmental influences (C'). *F* represents a composite environment that is due to maternal and paternal ADHD behavior levels. We allow maternal and paternal contributions to this family environment to differ with coefficients *m* and *p*, respectively. If the only source of family environmental influences is parental ADHD behaviors, C' is expected to be zero. If family environmental influences are unrelated to parental ADHD behaviors, *m* and *p* are expected to be zero.

With this model structure, two distinct sources of intergenerational transmission are represented. Children may resemble parents due to inheritance of genes contributing to ADHD behaviors (*A*), but they may also resemble parents due to the environment parents create (*F*). If ADHD behaviors are transmitted across generations both through genetic inheritance and the environment, genetic, and environmental effects on offspring ADHD behaviors will be correlated. If so, we assume that this process has been ongoing also in previous generations, represented by the correlation *w* between shared environmental and additive genetic effects in the parent generation. The *w* parameter is therefore constrained so that this gene–environment correlation is constant across generations.

All latent variables were scaled to have a total variance of one, except for *F* where the residual variance was set to zero. We allowed the observed variable means to differ across sexes and generations. However, in this model we assume that the parameters estimating environmental and genetic transmission are the same across sex.

Results

The measure of ADHD behaviors in the parent generation ranges from 1 to 5, and mothers had a mean score of 2.09 (S.D. = 0.57), while fathers had a mean score of 2.37 (S.D. = 0.53). In the offspring generation the measure of ADHD behaviors ranges from 1 to 4, and for the girls the mean was 1.4 (S.D. = 0.35), and for boys 1.54 (S.D. = 0.43).

Children's ADHD behaviors correlated 0.24 with their mothers' ADHD behaviors and 0.10 with their fathers' ADHD behaviors. ADHD behaviors between parents correlated 0.10. ADHD behaviors correlated at 0.35 for the monozygotic twins, while it was 0.23 for the dizygotic twins. The dizygotic twin correlation is more than half of the monozygotic correlation, suggesting that a model including shared environmental effects (ACE) is more appropriate than a model that estimates dominance instead (Additive genetics; Dominance; Unique environment (ADE)). The children-of-twins-and-siblings model provides estimates (given in Tables 1 and 2) for the sources of individual differences in (1) the parent generation and (2) the child generation, and (3) the degree to which parent–offspring correlation is due to genetic and/or environmental transmission.

Table 1 shows all the sources of variation in both the parental and offspring generation for full-scale ADHD, and the inattention and hyperactivity subscales. Additive genetic effects (*A*) accounted for 22% of the variability in parental ADHD behaviors. We found no indication of shared environmental effects (*C*) for

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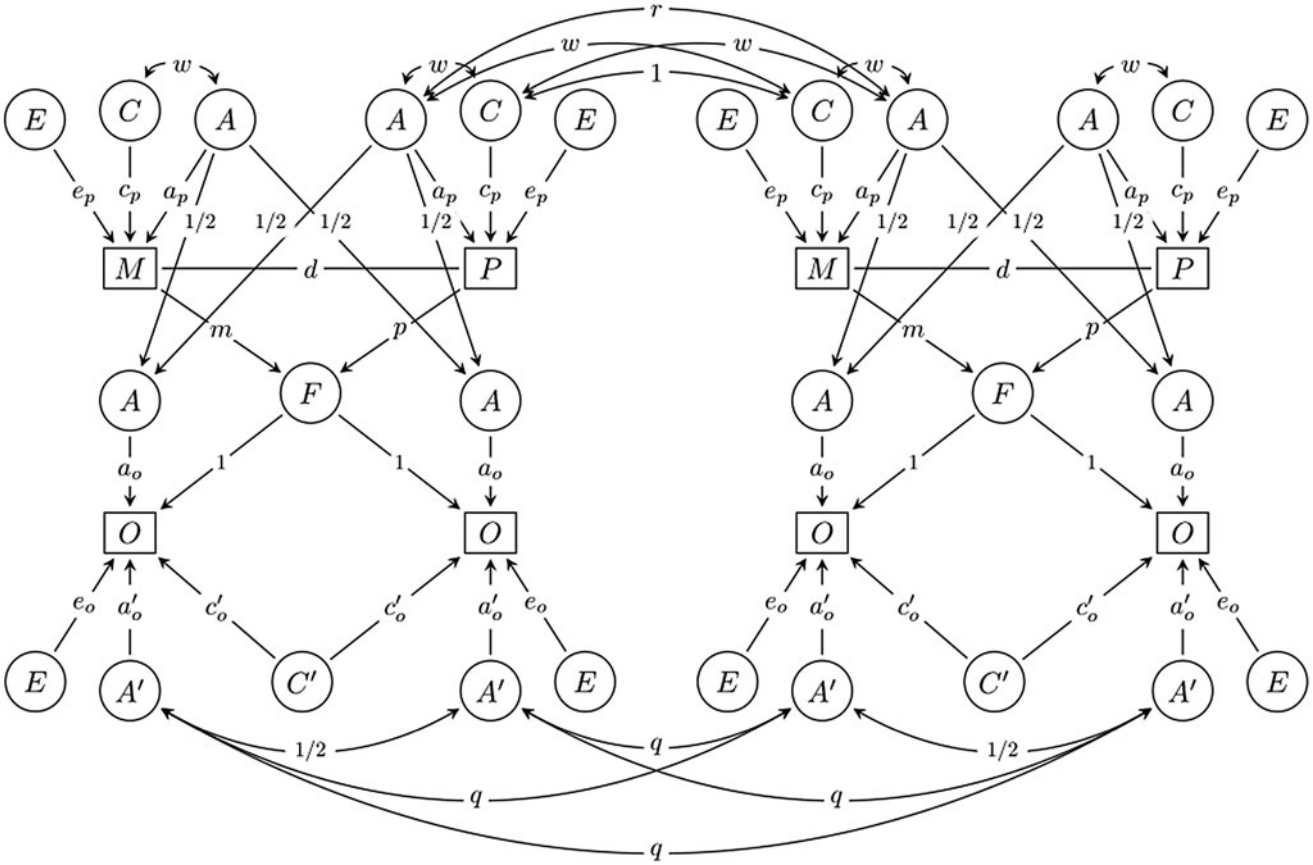

Figure 1. Children-of-twins-and-siblings model for one nuclear family. *Note*: This path diagram shows the features of the children-of-twins-and-siblings model. The modeling is based on two nuclear families, joined by e.g. a father and his sister. The rectangles represent measured maternal, paternal, and offspring ADHD behaviors, labeled *M*, *P*, and *O*, respectively. Latent variables are depicted by circles. *A*, additive genetics; *C*, shared environment; *E*, unique environment + measurement error; *F*, direct environmental effects (both maternal and paternal); *d*, partner covariance. a_p, additive genetic effects among parents; c_p, shared environment among parents; e_p, unique environment among parents; *d*, parental phenotypic covariance; *m*, maternal direct environmental effects; *p*, paternal direct environmental effects; *r*, genetic correlation between twins/siblings; *w*, gene–environment correlation in the parental generation; a_o, additive genetic effects shared between parents and offspring; a_o', genetic effects specific to offspring; c_o', shared environmental effects specific to offspring; e_o, unique environmental effects specific to offspring.

adult ADHD, whereas environmental effects specific to the individual (*E*) accounted for 78%. For offspring, additive genetic effects ($A + A'$) accounted for 57% of the variation. We found no effect of shared environment specific to the child generation (C'), whereas unique-environmental effects (*E*) were estimated at 38%.

Focusing on the association between parent and child ADHD behaviors, 11% of the phenotypic variation in child ADHD was due to genetic factors active in both generations (*A*), whereas 46% of the phenotypic variation was due to genetic factors specifically influencing children (A'). This corresponds to a genetic correlation of 0.44 between parent and offspring ADHD behaviors (calculated as the genetic covariance divided by the square root of the product of the heritabilities for parent and child ADHD behaviors). For offspring ADHD behaviors, approximately 2% of the variability was attributable to the direct environmental effect of parental ADHD behaviors (*F*). This minor effect was only due to the mother. Fathers did not contribute to environmental covariation across the generations. An additional 3% of the variability in offspring ADHD behaviors was accounted for by the correlation between the genetic and environmental effects transmitted from parental ADHD behaviors. All the estimates with standard errors are available in Table 2, including estimates for the inattention and hyperactivity subscales.

Most of the standard errors for the parameter estimates in Table 2 are small. However, for full-scale ADHD there are three exceptions: the shared environmental effect specific to the parents (c_p; 0.156), the shared environmental effect specific to the children (c_o'; 0.302), as well as the direct genetic effect from parents to offspring (a_o; 0.152). This suggests that these three parameters are more difficult to estimate precisely.

As can be seen in Fig. 2, child-specific genetic and unique environmental effects contribute to the majority of variance explained in children's full-scale ADHD behaviors. This is also the case when considering the inattention and hyperactivity subscales by themselves.

Discussion

Our results indicated that the intergenerational transmission of ADHD behaviors was mainly genetic in nature. That is, parents and children resembled each other in ADHD behaviors because they share genes. Parental ADHD behaviors had little or no correlation with their children's ADHD behaviors after their genetic resemblance was accounted for. Zooming in on the child level,

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Table 1. Decomposition of variance in ADHD behaviors

Source	Full ADHD scale (%)	Inattention subscale (%)	Hyperactivity subscale (%)
Parents			
A (additive genetics)	22	22	22
C (shared environment)	0	0	0
AC (gene–environment correlation)	0	0	0
E (unique environment)	78	78	78
Children			
A (genetics shared with parents)	11	7	10
A' (child-specific genetics)	46	35	29
F (direct environmental transmission)	2	2	2
C' (shared environment)	0	0	5
AF (gene–environment correlation)	3	2	2
E (unique environment)	38	53	54

variation in children's ADHD behaviors was driven by genetic influences shared with parents, as well as genetic and environmental influences unique to the child, but not by environmental influences from or shared with family members.

Our results strengthen and triangulate recent findings using different methods. For example, de Zeeuw et al. (2020) calculated separate adult polygenic scores for ADHD behaviors based on which genetic variants were transmitted *v.* not transmitted to the offspring. If the non-transmitted genetic variants predict offspring ADHD behaviors, it suggests that parental ADHD behaviors influence offspring beyond the inherited genetic variants (called 'genetic nurture' or 'dynastic effects'). They found no such effect. While their design cannot rule out environmental transmission because polygenic scores only capture a small proportion of the total genetic variance, our results – which should capture all genetic variance – strengthen their conclusion that the effect of genetic nurture from parental ADHD behaviors to child ADHD behaviors is close to zero. Although parental ADHD seems to have no environmental effect on offspring ADHD, future studies should investigate whether other parental traits do. There could be other parental traits beside ADHD that have a direct environmental effect on children's ADHD levels (Eilertsen et al., 2022). For example, a study that used the same sample and model as the present study found that parental education seemed to have a small environmental effect on offspring ADHD (Torvik et al., 2020). Another relevant finding is that low family income was associated with the development of ADHD behaviors in children, even for siblings within the same family that were exposed to different levels of family income (Larsson et al., 2014). Nevertheless, parental influences on child ADHD are likely to be small, given that twin and adoption studies do not find substantive effects of the shared environment on ADHD (Brikell et al., 2015; Franke et al., 2012; Nikolas & Burt, 2010).

Our findings are inconsistent with the idea that ADHD in children is influenced by the parenting styles often observed in parents with ADHD. And they are also inconsistent with psychological life-history theories postulating that parental ADHD behaviors serve to calibrate children's ADHD behaviors (Del Giudice, 2014; Frederick, 2012). Our findings are not consistent with environmental theories for two reasons. First, the parent–child resemblance for ADHD was due to transmitted genes, not parental ADHD. Second, the non-genetic component of variation in children's ADHD was almost entirely due to environmental influences unique to the child (E) rather than environmental influences from or shared with family members. This is inconsistent with environmental explanations that focus on parental ADHD and the parenting styles associated with it. Growing evidence now suggests that this unique environmental component is largely driven by inherent randomness during neural development (Mitchell, 2018; Tikhodeyev & Shcherbakova, 2019), rather than unique experiences. Random neurodevelopmental changes can disrupt cognitive development, such as neural mechanisms responsible for attention and impulse-control.

Taken together, this evidence suggests that ADHD is properly understood as a disorder and not an evolutionary adaptation (Kennair, Kleppestø, Jørgensen, & Larsen, 2018; Nesse, 2011; Wakefield, 1992). Other results are also consistent with this view. For example, ADHD portrays a high degree of comorbidity with other disorders, and studies have identified the cause for this comorbidity to be mostly shared genetic etiology (Byrne et al., 2020; Demontis et al., 2019; van Hulzen et al., 2017). This indicates that ADHD might share some molecular basis with schizophrenia, bipolar disorder, autism, major depression, and several other disorders, including many somatic diseases (see Instanes, Klungsøyr, Halmøy, Fasmer, & Haavik, 2018). If the genetic variants that are responsible for the ADHD heritability are numerous and have pleiotropic effects on other disorders, it would be consistent with the concept of ADHD as a maladaptive extreme of a continuum (Keller & Miller, 2006; Kennair et al., 2018; Nesse, 2011; Zietsch, de Candia, & Keller, 2015). In other words, from both a genetic and environmental point of view, ADHD seems to reflect a general neurodevelopmental vulnerability that is generated by varying degrees of genetic risk *and* developmental idiosyncrasies (Keller & Miller, 2006; Tikhodeyev & Shcherbakova, 2019; Zietsch et al., 2015).

Note that our conclusion that ADHD is not driven by environmental transmission such as the ones prescribed in life-history theories, is in line with recent critiques of life-history theory as a framework for human individual differences. If developmental adaptations evolved to be sensitive to parental cues and calibrated children's impulsivity, hyperactivity, and inattention accordingly, we would expect that the variance component that captures direct parental effects of ADHD in the children-of-twins-and-siblings model would explain much more variability in children's ADHD behaviors than it does.

Strengths and limitations

The children-of-twins-and-siblings model is ideal to study the effect of children's rearing environments, because it is a

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Table 2. Parameter estimates and standard error from the fitted models

	Full			Inattention			Hyperactivity		
Parameter	Est.	S.E.	Std. est.	Est.	S.E.	Std. est.	Est.	S.E.	Std. est.
Parents									
a_p	0.442	0.037	0.468	0.441	0.037	0.466	0.442	0.037	0.467
c_p	0.000	0.156	0.000	0.000	0.166	0.000	0.000	0.170	0.000
e_p	0.836	0.019	0.836	0.836	0.019	0.836	0.836	0.019	0.836
d	0.082	0.011	0.091	0.081	0.011	0.091	0.082	0.011	0.091
Children									
m	0.174	0.039	0.152	0.166	0.038	0.148	0.147	0.043	0.127
p	0.007	0.041	0.006	0.021	0.040	0.019	−0.008	0.045	−0.007
a_o	0.359	0.152	0.333	0.280	0.148	0.265	0.339	0.169	0.311
a'_o	0.732	0.070	0.679	0.629	0.069	0.594	0.584	0.195	0.535
c'_o	0.000	0.302	0.000	0.000	0.151	0.000	0.234	0.246	0.214
e_o	0.662	0.042	0.614	0.771	0.036	0.729	0.800	0.070	0.732

Note: a_p, additive genetic effects among parents; c_p, shared environment among parents; e_p, unique environment among parents; d, parental phenotypic covariance; m, maternal direct environmental effects; p, paternal direct environmental effects; a_o, additive genetic effects shared between parents and offspring; a'_o, genetic effects specific to offspring; c'_o, shared environmental effects specific to offspring; e_o, unique environmental effects specific to offspring; Std. est., standardized effects with all variables having a variance of 1.

quasi-experimental quantitative genetic design, capable of modeling most sources of genetic and environmental variance. Unlike the classical twin design, which assumes that genetic and environmental factors are uncorrelated, the children-of-twins-and-siblings model can estimate gene–environment correlation. This correlation contributed here 3% to children's ADHD behaviors. Further, the model investigates family level factors while controlling for genetic effects. It can also disentangle genetic effects shared across generations and genetic effects that are unique to children (McAdams et al., 2018). The advantage compared to other designs such as polygenic scores of transmitted and non-transmitted genetic variants (the 'genetic nurture' approach) is that the model

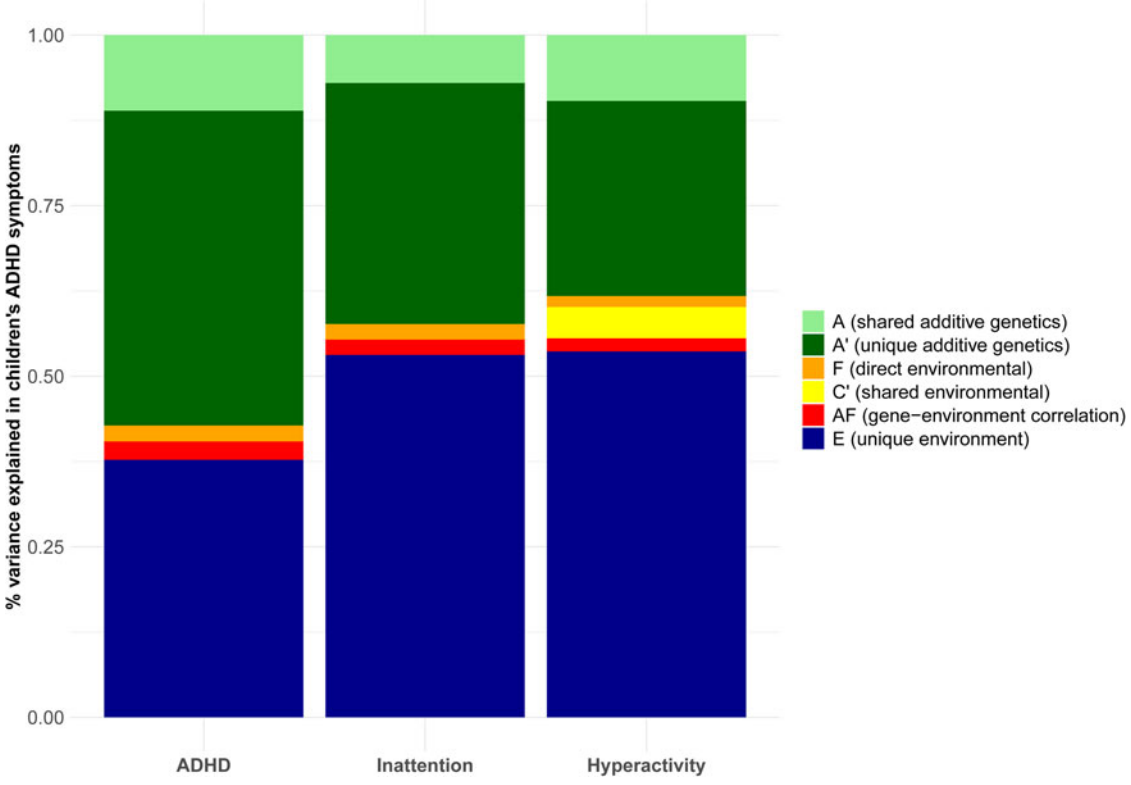

Figure 2. Visualization of variance decomposition.
Note: ADHD, full-scale ADHD; Inattention, inattention subscale; Hyperactivity, hyperactivity subscale.

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captures all genetic and environmental variance, not just a small fraction of it.

Although the children-of-twins-and-siblings model is uniquely qualified for investigating several different sources of variation at once, it also has some limitations (McAdams et al., 2018). One is less statistical power in detecting offspring effects, compared to parental effects. In the offspring generation, the cousins share only ~25% of their genes when their parents are monozygotic pairs, and only ~12.5% when their parents are dizygotic (or regular full siblings) pairs. These genetic-relatedness coefficients are lower than those in the adult generation (100% and 50%). This is reflected in our results, with for example a relatively high standard error for the child-specific shared environmental effect ($c'_o = 0.00$; S.E. = 0.302), despite our large sample. Furthermore, we had fewer siblings in the offspring generation (1445 pairs compared to 9442 in the adult generation), which also contributes to more uncertainty in the child-specific shared environmental estimate. People with high socioeconomic status were more likely to participate in MoBa and in the follow-up data collection (see Biele et al., 2019). Our sample therefore portray some selection bias in the sense of being more socioeconomically narrow than the general Norwegian population, which could compromise the generalizability of our findings. However, the differences in the ADHD proportion in MoBa and the general Norwegian population are small, suggesting reasonable generalizability for ADHD (Oerbeck et al., 2017). Future genetically sensitive population studies across different cultures and socioeconomic ranges will be informative.

We find that maternal ADHD behaviors have a tiny direct environmental effect on their children, corresponding to 2% explained variation in child ADHD behaviors. This effect was absent for fathers. A higher association between mothers and offspring ADHD compared to fathers and offspring ADHD have been reported in a population-based study (Solberg et al., 2021), suggesting the existence of sex-specific risk factors for ADHD behaviors. One possibility is that the parental effect is only significant for mothers because mothers tend to spend more time with their children than fathers. However, this small effect could also be artificial. Mothers, not fathers, rated their child's ADHD behaviors. Hence, the small mother-on-child effect could be due to rater bias, as mothers may have a consistent response style in scoring both their own and their child's ADHD behaviors. We recommend that future studies incorporate multiple informants on children's ADHD to circumvent this potential bias.

Our model allowed for sex differences in the mean level of ADHD behaviors, but we did not model potential sex differences in the biometric parameters. This is because doing so would increase the complexity of the model and the uncertainty of the parameters that are our main interest here, genetic and environmental transmission. However, future studies with an even larger sample size should consider the possibility that genetic and environmental transmission could differ across sex (e.g. potential differences in the impact of genetic transmission of ADHD behaviors from fathers and mothers).

In the parent generation, genetic variance explained 22% of variability in ADHD, while the unique environment explained 78%. Adult ADHD heritability is usually much lower than children's heritability. For example, Boomsma et al. (2010) estimated adult ADHD behaviors at 30%, based on a sample of 12 000, an estimate that echoes several others (Brikell et al., 2015). The differences in heritability for ADHD in children and adults might be due to ADHD having different genetic influences over time (Eilertsen et al., 2018). The genetic correlation between parent ADHD and child ADHD was only 0.44, which could mean that childhood ADHD is a fundamentally different phenotype than adult ADHD.

However, in a review of adult ADHD heritability (Brikell et al., 2015), the authors found that the heritability estimate drops precisely at the point where the ADHD measurements changes from using one rater of twin pairs (e.g. a parent or a teacher) to the adolescents rating themselves. Further, the adult ADHD heritability estimate is comparable to the estimate in children when adults are rated by other informants, suggesting that differences in the heritability estimates is due to differences in measurement quality, rather than developmental differences (see Brikell et al., 2015). This is also a plausible explanation for the differences in heritability for adults and children in our sample, parents in MoBa rated their own ADHD behaviors with only six items ($\alpha = 0.70$). A low adult heritability estimate and a low genetic correlation might reflect higher measurement error in the adult generation. This will likely underestimate intergenerational transmission.

Another potential source of bias is that the ADHD behaviors in parents and their children were obtained at different timepoints (fathers during the pregnancy, mothers when the children were ~3 years old, and the children when they were ~8 years old). Future genetically sensitive studies that measure ADHD in both parents and their children at the same time would be illuminating because our findings cannot rule out the important possibility that children's ADHD behaviors evoke parental ADHD behaviors. Another caveat is that parents that were half-siblings were modeled with the same amount of shared environment as full siblings. This could underestimate the shared environment in parental ADHD behaviors.

It is important to keep in mind that our findings reflect the natural situation, not what could be the case given effective interventions (van Bergen et al., 2018). That is, in the natural situation parents' ADHD behavior does not seem to impact children's ADHD behavior, but that does not rule out that active interventions at the parental level could induce changes in the offspring level. Indeed, parenting interventions for reducing children's ADHD symptoms have shown some effectiveness (Coates, Taylor, & Sayal, 2015).

Conclusion

Our study indicates that passive transmission of genetic factors explains the parent–child resemblance in ADHD behaviors. Children tend to resemble their parents in levels of impulsiveness, hyperactivity and (in)attention because of shared genetic influences, not because of shared home environments or effects of parental ADHD on child ADHD. Non-genetic factors play an important role in the development of ADHD, but these factors are largely unique to each child.

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Ethical standards. MoBa has been approved by the Regional Committees for Medical and Health Research Ethics and the Norwegian Data Inspectorate. The present study has approval no. 2013/863.

References

American Psychiatric Association (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Arlington: American Psychiatric Publishing.

Belsky, J., Steinberg, L., & Draper, P. (1991). Childhood experience, interpersonal development, and reproductive strategy: An evolutionary theory of socialization. *Child Development*, *62*(4), 647–670. doi:10.2307/1131166.

Berg, V., Kuja-Halkola, R., D'Onofrio, B. M., Lichtenstein, P., & Latvala, A. (2021). Parental substance misuse and reproductive timing in offspring: A genetically informed study. *Evolution and Human Behavior*, *42*(2), 157–164.

Biele, G., Gustavson, K., Czajkowski, N. O., Nilsen, R. M., Reichborn-Kjennerud, T., Magnus, P. M., … Aase, H. (2019). Bias from self selection and loss to follow-up in prospective cohort studies. *European Journal of Epidemiology*, *34*(10), 927–938.

Boomsma, D. I., Saviouk, V., Hottenga, J.-J., Distel, M. A., De Moor, M. H., Vink, J. M., … de Geus, E. J. (2010). Genetic epidemiology of attention deficit hyperactivity disorder (ADHD index) in adults. *PLoS ONE*, *5*(5), e10621.

Brikell, I., Kuja-Halkola, R., & Larsson, H. (2015). Heritability of attention-deficit hyperactivity disorder in adults. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics*, *168*(6), 406–413.

Byrne, E. M., Zhu, Z., Qi, T., Skene, N. G., Bryois, J., Pardinas, A. F., … Owen, M. J. (2020). Conditional GWAS analysis to identify disorder-specific SNPs for psychiatric disorders. *Molecular Psychiatry*, *26*(6), 2070–2081.

Coates, J., Taylor, J. A., & Sayal, K. (2015). Parenting interventions for ADHD: A systematic literature review and meta-analysis. *Journal of Attention Disorders*, *19*(10), 831–843.

Del Giudice, M. (2014). An evolutionary life history framework for psychopathology. *Psychological Inquiry*, *25*, 261–300.

Demontis, D., Walters, R. K., Martin, J., Mattheisen, M., Als, T. D., Agerbo, E., … Bækvad-Hansen, M. (2019). Discovery of the first genome-wide significant risk loci for attention deficit/hyperactivity disorder. *Nature Genetics*, *51*(1), 63–75.

de Zeeuw, E. L., Hottenga, J.-J., Ouwens, K. G., Dolan, C. V., Ehli, E. A., Davies, G. E., … van Bergen, E. (2020). Intergenerational transmission of education and ADHD: Effects of parental genotypes. *Behavior Genetics*, *50*, 221–232.

D'Onofrio, B. M., Turkheimer, E. N., Eaves, L. J., Corey, L. A., Berg, K., Solaas, M. H., & Emery, R. E. (2003). The role of the children of twins design in elucidating causal relations between parent characteristics and child outcomes. *Journal of Child Psychology and Psychiatry*, *44*(8), 1130–1144.

Eilertsen, E. M., Cheesman, R., Ayorech, Z., Røysamb, E., Pingault, J. B., Njølstad, P. R., … Torvik, F. A. (2022). On the importance of parenting in externalizing disorders: An evaluation of indirect genetic effects in families. *Journal of Child Psychology and Psychiatry*, *63*(10), 1186–1195.

Eilertsen, E. M., Gjerde, L. C., Kendler, K. S., Røysamb, E., Aggen, S. H., Gustavson, K., … Ystrom, E. (2018). Development of ADHD symptoms in preschool children: Genetic and environmental contributions. *Development and Psychopathology*, *31*(4), 1299–1305. doi:10.1017/S0954579418000731.

Franke, B., Faraone, S. V., Asherson, P., Buitelaar, J., Bau, C. H. D., Ramos-Quiroga, J. A., … Reif, A. (2012). The genetics of attention deficit/hyperactivity disorder in adults, a review. *Molecular Psychiatry*, *17*(10), 960–987.

Frederick, M. J. (2012). Birth weight predicts scores on the ADHD self-report scale and attitudes towards casual sex in college men: A short-term life history strategy? *Evolutionary Psychology*, *10*(2), 147470491201000212.

Hart, S. A., Little, C., & Van Bergen, E. (2021). Nurture might be nature: Cautionary tales and proposed solutions. *NPJ Science of Learning*, *6*(1), 1–12.

Instanes, J. T., Klungsøyr, K., Halmøy, A., Fasmer, O. B., & Haavik, J. (2018). Adult ADHD and comorbid somatic disease: A systematic literature review. *Journal of Attention Disorders*, *22*(3), 203–228.

Keller, M. C., & Miller, G. (2006). Resolving the paradox of common, harmful, heritable mental disorders: Which evolutionary genetic models work best? *Behavioral and Brain Sciences*, *29*(4), 385–404. doi:10.1017/S0140525X06009095.

Kennair, L. E. O., Kleppestø, T. H., Jørgensen, B. E. G., & Larsen, S. M. (2018). Evolutionary clinical psychology. In T. K. Shackelford & V. A. Weekes-Shackelford (Eds.), *Encyclopedia of evolutionary psychological science* (pp. 1–14). Cham: Springer International Publishing.

Kessler, R. C., Adler, L., Ames, M., Demler, O., Faraone, S., Hiripi, E. V. A., … Walters, E. E. (2005). The World Health Organization adult ADHD self-report scale (ASRS): A short screening scale for use in the general population. *Psychological Medicine*, *35*(2), 245–256. doi:10.1017/s0033291704002892.

Larsson, H., Sariaslan, A., Långström, N., D'Onofrio, B., & Lichtenstein, P. (2014). Family income in early childhood and subsequent attention deficit/hyperactivity disorder: A quasi-experimental study. *Journal of Child Psychology and Psychiatry*, *55*(5), 428–435.

Magnus, P., Birke, C., Vejrup, K., Haugan, A., Alsaker, E., Daltveit, A. K., … Stoltenberg, C. (2016). Cohort profile update: The Norwegian mother and child cohort study (MoBa). *International Journal of Epidemiology*, *45*(2), 382–388. doi:10.1093/ije/dyw029.

McAdams, T. A., Hannigan, L. J., Eilertsen, E. M., Gjerde, L. C., Ystrom, E., & Rijsdijk, F. V. (2018). Revisiting the children-of-twins design: Improving existing models for the exploration of intergenerational associations. *Behavior Genetics*, *48*(5), 397–412.

McAdams, T. A., Neiderhiser, J. M., Rijsdijk, F. V., Narusyte, J., Lichtenstein, P., & Eley, T. C. (2014). Accounting for genetic and environmental confounds in associations between parent and child characteristics: A systematic review of children-of-twins studies. *Psychological Bulletin*, *140*(4), 1138–1173. Retrieved from http://psycnet.apa.org/journals/bul/140/4/1138.pdf.

Miller, L. L., Gustafsson, H. C., Tipsord, J., Song, M., Nousen, E., Dieckmann, N., & Nigg, J. T. (2018). Is the association of ADHD with socio-economic disadvantage explained by child comorbid externalizing problems or parent ADHD? *Journal of Abnormal Child Psychology*, *46*, 951–963.

Mitchell, K. J. (2018). *Innate: How the wiring of our brains shapes who we are*. New Jersey: Princeton University Press.

Neale, M. C., & Maes, H. H. M. (2004). *Methodology for genetic studies of twins and families*. Dordrecht, The Netherlands: Kluwer Academic Publishers B.V.

Nesse, R. M. (2011). Ten questions for evolutionary studies of disease vulnerability. *Evolutionary Applications*, *4*(2), 264–277. doi:10.1111/j.1752-4571.2010.00181.x.

Nettle, D., & Frankenhuis, W. E. (2020). Life-history theory in psychology and evolutionary biology: One research programme or two? *Philosophical Transactions of the Royal Society B*, *375*(1803), 20190490.

Nikolas, M. A., & Burt, S. A. (2010). Genetic and environmental influences on ADHD symptom dimensions of inattention and hyperactivity: A meta-analysis. *Journal of Abnormal Psychology*, *119*(1), 1.

Oerbeck, B., Overgaard, K. R., Aspenes, S. T., Pripp, A. H., Mordre, M., Aase, H., … Zeiner, P. (2017). ADHD, comorbid disorders and psychosocial functioning: How representative is a child cohort study? Findings from a national patient registry. *BMC Psychiatry*, *17*, 1–9.

Park, J. L., Hudec, K. L., & Johnston, C. (2017). Parental ADHD symptoms and parenting behaviors: A meta-analytic review. *Clinical Psychology Review*, *56*, 25–39.

Pingault, J.-B., Barkhuizen, W., Wang, B., Hannigan, L. J., Eilertsen, E. M., Corfield, E., … Havdahl, A. (2023). Genetic nurture versus genetic transmission of risk for ADHD traits in the Norwegian Mother, Father and Child Cohort Study. *Molecular Psychiatry*, *28*(4), 1731–1738. doi:10.1038/s41380-022-01863-6.

Sheppard, P., & Van Winkle, Z. (2020). Using sequence analysis to test if human life histories are coherent strategies. *Evolutionary Human Sciences*, *2*, 1–18.

Silberg, J. L., Maes, H., & Eaves, L. J. (2010). Genetic and environmental influences on the transmission of parental depression to children's depression and conduct disturbance: An extended children of twins study. *Journal of Child Psychology and Psychiatry*, *51*(6), 734–744.

https://doi.org/10.1017/S003329172300315X Published online by Cambridge University Press

Silva, R. R., Alpert, M., Pouget, E., Silva, V., Trosper, S., Reyes, K., & Dummit, S. (2005). A rating scale for disruptive behavior disorders, based on the DSM-IV item pool. *Psychiatric Quarterly*, *76*(4), 327–339.

Solberg, B. S., Hegvik, T. A., Halmøy, A., Skjærven, R., Engeland, A., Haavik, J., & Klungsøyr, K. (2021). Sex differences in parent–offspring recurrence of attention-deficit/hyperactivity disorder. *Journal of Child Psychology and Psychiatry*, *62*(8), 1010–1018.

Sonuga-Barke, E. J., Becker, S. P., Bölte, S., Castellanos, F. X., Franke, B., Newcorn, J. H., … Simonoff, E. (2023). Annual Research Review: Perspectives on progress in ADHD science – From characterization to cause. *Journal of Child Psychology and Psychiatry*, *64*(4), 506–532.

Tikhodeyev, O. N., & Shcherbakova, OV (2019). The problem of non-shared environment in behavioral genetics. *Behavior Genetics*, *49*(3), 259–269.

Torvik, F. A., Eilertsen, E. M., McAdams, T. A., Gustavson, K., Zachrisson, H. D., Brandlistuen, R., … Ask, H. (2020). Mechanisms linking parental educational attainment with child ADHD, depression, and academic problems: A study of extended families in The Norwegian Mother, Father and Child Cohort Study. *Journal of Child Psychology and Psychiatry*, *61*(9), 1009–1018.

Tung, I., Brammer, W. A., Li, J. J., & Lee, S. S. (2015). Parenting behavior mediates the intergenerational association of parent and child offspring ADHD symptoms. *Journal of Clinical Child & Adolescent Psychology*, *44*(5), 787–799.

van Bergen, E., Snowling, M. J., de Zeeuw, E. L., van Beijsterveldt, C. E., Dolan, C. V., & Boomsma, D. I. (2018). Why do children read more? The influence of reading ability on voluntary reading practices. *Journal of Child Psychology and Psychiatry*, *59*(11), 1205–1214.

van Hulzen, K. J., Scholz, C. J., Franke, B., Ripke, S., Klein, M., McQuillin, A., … Andreassen, O. A. (2017). Genetic overlap between attention-deficit/hyperactivity disorder and bipolar disorder: Evidence from genome-wide association study meta-analysis. *Biological Psychiatry*, *82*(9), 634–641.

Wakefield, J. C. (1992). Disorder as harmful dysfunction: A conceptual critique of DSM-III--R's definition of mental disorder. *Psychological Review*, *99*, 232–247. doi:10.1037//0033-295X.99.2.232.

Zietsch, B. P., de Candia, T. R., & Keller, M. C. (2015). Evolutionary behavioral genetics. *Current Opinion in Behavioral Sciences*, *2*, 73–80.

Zietsch, B. P., & Sidari, M. J. (2020). A critique of life history approaches to human trait covariation. *Evolution and Human Behavior*, *41*(6), 527–535. https://doi.org/10.1016/j.evolhumbehav.2019.05.007.

https://doi.org/10.1017/S003329172300315X Published online by Cambridge University Press