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Genetic Confounding of the Relationship between Father Absence and Age at Menarche

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Abstract

Research in evolutionary psychology, and life history theory in particular, has yielded important insights into the developmental processes that underpin variation in growth, psychological functioning, and behavioral outcomes across individuals. Yet, there are methodological concerns that limit the ability to draw causal inferences about human development and psychological functioning within a life history framework. The current study used a simulation-based modeling approach to estimate the degree of genetic confounding in tests of a well-researched life history hypothesis: that father absence (*X*) is associated with earlier age at menarche (*Y*). The results demonstrate that the genetic correlation between *X* and *Y* can confound the phenotypic association between the two variables, even if the genetic correlation is small—suggesting that failure to control for the genetic correlation between *X* and *Y* could produce a spurious phenotypic correlation. We discuss the implications of these results for research on human life history, and highlight the utility of incorporating this genetically sensitivity tests into future life history research.

Keywords: Life history theory; age at menarche; father absence; behavioral genetics; simulation.

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1. Introduction

Researchers in the behavioral sciences have made theoretical and empirical advances by leveraging life history theory to better understand human psychology and behavior (e.g., Brumbach, & Scholmer, 2009; Chrisholm, 1993, 1999; Del Giudice, 2009; Figueredo, et al., 2006). Within this framework, life history theorists argue that aspects of the familial environment during childhood are associated with conditional adjustments of an individual's life history strategy. In particular, research has advanced the hypothesis that father absence in childhood is associated with earlier age at menarche (Belsky, Steinberg & Draper, 1991; Ellis, 2004; Ellis, Figueredo, Brumbach, & Schlomer, 2009; Mul, Oostdijk, & Drop, 2002; Parent et al., 2003). In the current article, we propose an alternative hypothesis: that the relationship between father absence and age at menarche is confounded by the genetic correlation between the two phenotypic traits. We suggest that the association between father absence and age at menarche may not reflect a causal association, but instead could result from a shared genetic variation. We provide support for this argument by employing simulation-based modeling to demonstrate the degree to which the phenotypic correlation (r_p) between father absence (X) and age at menarche (Y) might be confounded by genetic variation. We do so by drawing on estimates of r_p and on heritability coefficients for both X and Y that have been previously published.

1.1. Human Life History

Life history theory provides a framework for addressing how and why organisms, including humans, allocate resources to conflicting life tasks (Kaplan & Gangestad, 2005; Roff, 2002; Sterns, 1992). Allocating resources to these conflicting life tasks involves tradeoffs, because the available resources are finite and limited. Resources must be strategically allocated so that the organism can grow, maintain homeostasis, and reproduce. Resource allocation "decisions" are made throughout the lifespan and are reflected in an individual's behaviors (Kenrick, Girskevicius, Neuberg, & Shaller, 2010; Simpson, Griskevicius, & Kim, 2011). Allocation strategies that optimized the use of resources throughout the lifespan were selected over human evolutionary history (Ellis et al., 2009). Ancestrally adaptive resource

allocation strategies vary with species-typical evolutionary history, individual differences, and local ecology. Life history theorists argue that the solutions to life history tradeoffs arise via combination of genetic variation and environmental inputs experienced by the organism (Ellis et al., 2009), whereby psychological and physiological mechanisms "decide" how to allocate resources that enhanced ancestral survival and reproduction (Chrisholm, 1999).

Natural selection has produced a species-typical life history strategy in humans characterized by lengthy pregnancy, extended childhood, high parental investment, and low fecundity (Hawkes, 2006; Rushton, 2000). The question then becomes: what causes individual variation in resource allocation decisions and in the speed of life history strategies? Within-species variation in life history strategies is recognized across human populations and across diverse animal taxa (Gross, 1996; Promislow & Harvey, 1990; Roff, 2002; Sterns, 1992; West-Eberhard, 2003). Individual differences in life history strategies are facilitated by psychological and physiological mechanisms, underpinned by genes that are responsive to the local ecology and that afford conditional adjustments within the constraints of the species-typical life history strategy (Ellis et al., 2009).

Applications of life history theory to developmental psychology, in particular, center on the role of childhood environments calibrating life history traits that manifest across an individual's lifespan. Belsky and colleagues (1991) argue that aspects of the family environment in early childhood influence the reproductive strategies of females, in particular. Certain indicators of familial functioning, such as father absence, are hypothesized to result in earlier pubertal maturation, and specifically an earlier age at menarche in girls. Earlier age at menarche is thought to be indicative of a faster life history strategy in which greater resources are allocated to mating effort via the ability to begin reproduction at an earlier age (Belsky et al., 1991; Ellis, 2004). However, there remain two perspectives regarding the determinants of menarche timing: (1) Selection has favored psychological mechanisms that are sensitive to, for example, specific familial environmental inputs, which afford conditional adjustments of pubertal maturation and life history strategies, or (2) genetic variation accounts for individual differences in

pubertal maturation and life history strategies (i.e., the life history of an individual's genetic relatives is more indicative of the individual's life history strategy).

Age at menarche is a well-investigated life history trait (Ellis, 2004; Ellis, McFadyen-Ketchum, Dodge, Pettit, & Bates, 1999; Mul, Oostdijk, & Drop, 2002; Parent et al., 2003), with the prevailing hypothesis being that father absence—an aspect of the familial environment—results in earlier age of menarche, thereby facilitating the execution of a faster life history strategy. In accordance with the first perspective above, age at menarche is more strongly determined by environmental risk during development, such that earlier age at menarche may facilitate earlier reproduction and greater mating effort. In accordance with the second perspective above, however, age at menarche is heritable (Dick, Rose, Pulkkinen, & Kaprio, 2001; Kirk et al., 2001; Rowe, 2002), suggesting that individual variation in age at menarche may be more strongly influenced by one's genes, independent of father absence, specifically.

The degree to which environmental conditions or genetic variation are influential in determining menarche timing remains a topic of debate among life history theorists. If the second perspective is accurate—that is, genetic influences account for individual variation in age at menarche, independent of the early familial environment—it would not diminish the importance of the environment. Empirical evidence in accordance with the second perspective would, however, (1) necessitate research designs capable of holding genetic variation constant so that environmental influences on pubertal maturation in girls can be accurately investigated (see generally Barnes, Boutwell, Beaver, Gibson, & Wright, 2014), and (2) suggest that for age at menarche, specifically, father absence may not be as influential as previously suggested (see Ellis, 2004).

1.2. Genetic Influences on Pubertal Maturation in Girls

Although discussion and investigation of genetic factors contributing to individual variation in life history strategies is limited, researchers have called for an integration of life history theory and behavioral genetic methodologies (Ellis et al., 2009; Figueredo, Vasquez, Brumbach, & Schneider, 2004; Harkness, 2014; Hofmann, 2003; MacDonald, 1997; Scarr 1995). Behavioral genetics provides insight

into the genetic and environmental influences on human traits, which affords estimates of the phenotypic variation explained by genetic factors and environmental factors (Plomin, DeFries, Knopik, Neiderhiser, 2013). Phenotypic variance is composed of three factors: heritability (h^2), shared environment (c^2), and nonshared environment (e^2). The h^2 component refers to phenotypic variance accounted for by variance in genes.[1] The environmental components (c^2 and e^2) refer to phenotypic variance accounted for by environmental experiences shared with others (i.e., aspects of the environment that make people similar to one another, c^2) and environmental experiences not shared with others (i.e., aspects of the environment that make people dissimilar, e^2).

A growing number of studies have employed genetically sensitive research designs to address issues of genetic confounding when testing life history hypotheses (Dick et al., 2001; D'Onofrio et al., 2006; Ellis, Schlomer, Tilley, & Butler, 2012; Kirk et al., 2001; Mendle et al., 2006, 2009; Tither & Ellis, 2008; Rowe, 2002). The results have revealed that various traits directly related to life history strategies are moderately to highly heritable (e.g., age at menarche; Dick et al., 2001; Kirk et al., 2001), as are indirect measures of life history strategies (e.g., mother relationship quality; Figueredo et al., 2004). These findings present life history researchers with an important issue that requires consideration in future research.

Specifically, to the extent that genetic factors exert influence on population variance in life history strategies, ignoring genetic influences may bias research aimed at examining the environmental influences on human life history. Put differently, genetic variance underpinning phenotypic traits may be conflated with environmental variance when estimating the relationship between two phenotypes if that genetic variance is not held constant. Moreover, environmental experiences hypothesized to influence the manifestation of life history strategies do not occur at random (Scarr, 1995). Selection effects, underpinned by genes, exert an influence on the environments that humans experience via gene-

[1] Additive variance (V_A) is often indexed by h^2, so it is more accurate to describe this as evidence for "narrow-sense" heritability. With that in mind, Hill and colleagues (2008) provided evidence suggesting that additive variance accounts for the majority of genetic variance in many traits. Thus, the focus on additive variance is unlikely to bias h^2 estimates for many (if not most) phenotypes.

environment correlation (*r*GE) (Barnes et al., 2014; Kendler & Baker, 2007; Scarr & McKartney, 1983). Individuals seek out environments and experiences that correspond to their genotype, making it possible that environmental experiences are heritable due to an indirect effect of the genes on the environment that is mediated by individual decision making.[2] Failing to account for the influence of genetic variation on environmental conditions may impede the ability to draw accurate conclusions about which aspects of the environment *are* influential to individual variation in age at menarche. Because the influence of environmental factors on adolescent and adult sexual psychological and behavioral outcomes are a linchpin in life history theory, appropriate steps need to be taken to account for potential genetic confounding.

Research utilizing behavioral genetic methodologies have estimated the contribution of genetic variation and environmental inputs on pubertal maturation and reproductive traits, including age at menarche (D'Onofrio et al., 2006; Tither & Ellis, 2008), age at first reproduction (Kirk et al., 2001; Rowe, 2002), pubertal development (Dick et al., 2001), sexual debut (Mendle et al., 2009), and sexual behavior (D'Onofrio et al., 2006; Ellis et al., 2012). The results of these studies (reviewed below) demonstrate significant genetic contributions to the aforementioned life history traits—highlighting the potential for genetic confounding when life history traits are analyzed as outcome variables.

Kirk and colleagues (2001) conducted a twin study to estimate heritability for three life history traits in women: age at menarche, age at first reproduction, and age at menopause. The researchers estimated h^2 was 0.50 for age at menarche, 0.23 for age at first reproduction, and 0.45 for age at menopause. Similar estimates were reported in another twin study (Dick et al., 2001) in which h^2 estimates and c^2 estimates were calculated for a pubertal development factor that included several individual markers (e.g., body hair, breast change, menarche) at 12 years and 14 years. For girls, $h^2 = 0.40$

[2] Imagine a personality trait *P* emerges largely due to genetic factors. To the extent that *P* influences individuals' choices to engage in environmental situations, then those environmental factors will appear to be heritable due to the mediating role of *P* between the genes and the environment.

at age 12 and 0.68 at age 14, and $c^2 = 0.45$ at age 12 and 0.02 at age 14.[3] Other studies (see Rowe, 2002) reported similar estimates for age at menarche ($h^2 = 0.44$) and for pubertal timing in girls ($h^2 = 0.40$).

Several studies have utilized sibling and twin methodologies to account for genetic variation and environmental conditions to test life history hypotheses concerning pubertal maturation and sexual behavior. Tither and Ellis (2008) collected data from full siblings at least four years apart in age. Two groups of sibling pairs participated, affording within- and between-family comparisons. Sister pairs from intact families included sisters for which both had their genetic father present throughout childhood. Sister pairs from disrupted families included sisters in which the older sister had her genetic father present until about 12 years of age, but the younger sister only had her genetic father present until about age five. The study design allowed the researchers to examine the effect of father absence on age at menarche in sibling pairs, while partially controlling for the effects of shared genes. The results indicated that father absence due to divorce or separation caused younger sisters in father absent homes to attain menarche earlier than their own older sisters, and earlier than younger sisters from father present homes. These results offer suggestive evidence that father absence in childhood is influential on age at menarche (Tither & Ellis, 2008). But not all genetic variation can be accounted for by this research design.

The influence of genetic factors and environmental factors also was investigated in relation to risky sexual behavior in girls (Ellis et al., 2012). Using the sibling design (Tither & Ellis, 2008) afforded conclusions about whether familial environmental cues predicted risky sexual behavior after accounting for shared genetic variation. The results indicated that variation in risky sexual behavior of siblings did not differ with family constellation (disrupted vs. non-disrupted), indicating that father absence might not influence risky sexual behavior once genetic influences are held constant.

Comparing the children of sisters, Mendle and colleagues (2009) accounted for shared genetic factors while investigating the effect of unique home environments, specifically father absence, on age at sexual debut in both males and females. The results indicated that shared genetic variation, and not

[3] For boys, $h^2 = 0.74$ at age 12 and 0.92 at age 14, and $c^2 = 0.13$ at age 12 (c^2 at 14 years was not reported).

environmental conditions, accounted for the association between father absence and sexual debut. Controlling for a larger amount of genetic variation (i.e., children of twin sisters), age at sexual debut for the children that resided in father absent homes did not differ from age at sexual debut for the children that resided in father present homes.

Comparable results of genetic confounding were obtained by D'Onofrio et al. (2006). Using the children of twins research design, D'Onofrio et al. (2006) found no relationship between father absence and age at menarche (although there was an effect of father absence on sexual debut in this sample). Mendle et al. (2009) and D'Onofrio et al. (2006) note that genetic variation may account for the previously reported phenotypic associations between father absence on pubertal maturation, or that the association may be a result of *r*GE, in that the environments children experience are correlated with the genotypes that they inherit from their parents (Kendler & Baker, 2007). Both interpretations are consistent with the hypothesis that the relationship between father absence and age at menarche may be due to the genetic correlation between the two variables, and not due to a causal effect of father absence on age at menarche.

As previously stated, ignoring genetic influences on life history traits may bias research investigating environmental influences that are unassociated with the trait of interest once genetic variation is held constant. It is beyond dispute that environmental factors influence the expression of phenotypic traits, evidenced by the fact that for most traits, phenotypic variance is composed of approximately equal proportions of genetic variance and nonshared environmental variance (Bouchard & Loehlin, 2001; Polderman et al., 2015; Turkheimer, 2000). Research designs such as differential sibling-exposure designs (Ellis et al., 2012; Tither & Ellis, 2008) and children of sisters and twins designs (D'Onofrio et al. 2006; Mendle et al., 2009) have attempted to disentangle the sources of phenotypic variance in life history traits. It is important to note, however, that by only evaluating sibling pairs (Tither & 2008; Ellis et al., 2012), genetic variation cannot be fully controlled for as in classic twin studies, because siblings only share, on average, 50% of their genes. The children of sisters (Mendle et al., 2009) or twins (D'Onofrio et al. 2006) designs also cannot fully control for genetic variation. Moreover, the

children of siblings and twins designs are not capable of accounting for genetic influences of the mother's spouse, or other family-wide environmental confounds.

Classic twin studies (Dick et al. 2001; Kirk et al., 2001; Rowe, 2002) employed in behavioral genetics research, however, afford the greatest control of genetic variation and are best equipped to examine whether hypothesized environmental factors, such as father absence, affect menarche timing independent of genetic variation. The use of twin designs to estimate heritability and environmentality of age at menarche have been criticized, and we refer the reader to Ellis (2004) for a review of this position. Pertinent to the current discussion, if father absence does exert a meaningful effect on age at menarche, then there would be some indication of shared environmental effects (c^2) on age at menarche in twin studies, and this is not the case (Dick et al. 2001; Kirk et al., 2001; Rowe, 2002). Ellis (2004), however, contends that children (even assuming a twin design) may not experience father absence equally and, therefore, the differential sibling-exposure design (Tither & Ellis, 2008) can capture father absence as nonshared environmental effect (e^2), consistent with behavioral genetic evidence. The *experience of an absent father*, however, is not the same as *a father being absent*—the latter most often the measured variable in research studies, and which would show up as a shared environmental effect (c^2) (see Plomin et al., 2013). As reviewed above, however, these alternative genetically sensitive designs have yielded ambiguous and conflicting results regarding whether father absence exerts a meaningful effect on age at menarche, independent of genetic contributions (e.g., D'Onofrio et al. 2006; Tither & Ellis, 2008).

2. The Current Study

Sibling and twin research designs offer one way to investigate the extent to which father absence might exert a meaningful influence on menarche timing. Twin designs, in particular, are capable of parceling out genetic influences that cut across the independent (X) and dependent variable (Y). Although this approach is possible (e.g., Dick et al. 2001; Kirk et al., 2001; Rowe, 2002), significant resources are needed to execute twin and sibling studies, which might not always be feasible or available. Further, the difficulty of gathering data from twins or adopted children may limit the utility of these approaches for many investigators, and delay the dissemination of important research findings. Other alternative

approaches, such as the re-analysis of secondary datasets, often do not afford the opportunity to fit biometric twin models, and such datasets often do not contain the necessary well-validated life history measures needed to accurately test life history hypotheses (e.g., Add Health, although a rich data source, does not include specific life history measures; Harris et al., 2003).

Another approach to investigate the association between familial functioning and pubertal maturation is via simulation-based modeling. Barnes and colleagues (2014) provide a framework for estimating genetic confounding using a series of simulated datasets to estimate the degree to which uncontrolled genetic factors can bias data that are not genetically sensitive. The results suggest that if the phenotypic correlation between *X* and *Y* is large in magnitude, genetic influences pose less of a problem in terms of rendering that correlation spurious. This was not the case, however, as the genetic effect on the two variables increased to reflect a moderate and realistic heritability estimate. Failure to account for genetic influences that impact independent and dependent variables of interest may produce spurious results mistaken to be evidence of causal association.

The use of simulation-based modeling provide a powerful, accessible, and convenient companion to the genetically sensitive research designs discussed above. The current study focuses on the life history hypothesis concerning the association between father absence (*X*) and age at menarche (*Y*). The current study employs a simulation-based modeling procedure to investigate the extent to which father absence exerts an influence on age at menarche, independent of genetic influences. The findings provide a barometer for the degree to which previous and future life history studies risk confounding of phenotypic associations when genetically controlled research designs are not (or cannot be) implemented. The current study examines the extent to which there is genetic confounding of the association between father absence and age at menarche.

2.1. Plan of Analysis

The statistical tool introduced in the current article is underpinned by the logic of Bayesian statistical analysis and simulation (Gelman et al., 2014). Formal details of the simulation tool are provided in the Appendix. The goal of the approach is simple: estimate the degree to which unmeasured

genetic factors might account for the observed correlation between the two phenotypic traits of *X* (father absence) and *Y* (age at menarche), if genetically sensitive data are unavailable. Four pieces of information are needed to conduct the simulation to produce estimates of the degree of genetic confounding that may account for the observed phenotypic correlation. First, one must specify the heritability of *X* (h^2_X) (i.e., the heritability of father absence). Second, one must specify the heritability of *Y* (h^2_Y) (i.e., the heritability of age at menarche). Third, one must specify the correlation between the two phenotypes (r_p). And fourth, one must specify the *genetic* correlation between the two phenotypes (r_g). The genetic correlation (r_g) between two phenotypes refers to the extent to which genetic variations that affect X correlate with the genetic variation that affect Y (Plomin et al., 2013)—analogous to the "third variable problem." These four inputs are entered into the equation below to provide an estimate of the degree to which the phenotypic correlation covaries with genetic effects, where h^2_{cov} represents the degree to which the covariance between *X* and *Y* is due to genetic factors when other parameters are as specified.

$$h^2_{\text{cov}} = \frac{\sqrt{h^2_X} * r_g * \sqrt{h^2_Y}}{r_p}$$

Heritability estimates for almost any trait can be derived from the behavioral genetic literature (Plomin et al., 2013; Polderman et al., 2015). One can derive estimates for h^2_X and h^2_Y simply by consulting the available literature. Similarly, the range of values for r_p can be derived by consulting the available literature, which leaves only r_g to be identified. Because precise estimations of r_g requires genetic analyses of many families each with a large number of progeny, values of r_g are often hard to come by. Thus, we recommend drawing on a range of values that are plausible, yet conservative, based on the other available evidence. We follow this strategy in the present analysis.

Recognizing that there is not one "true" fixed heritability estimate for any particular trait (heritability estimates can fluctuate across ecological and historical conditions), the simulation procedure is most informative if one secures a reasonable estimation of the average heritability estimate, *in addition*

to the range of expected heritability estimates. Put differently, one is not expected to provide exact values for h^2_X, h^2_Y, r_p, or r_g. Our approach, therefore, is to provide a *distribution* of possible values for each of the components of the above h^2_{cov} equation. The simulation procedure samples from the specified distributions, and solves the above equation for h^2_{cov} with those sampled values. This process is repeated k times, where k is supplied by the user. k is set to 10,000 for this analysis.

The mechanism for providing possible solutions across a range of parameter estimates (to account for the most likely values for each of the parameters entered into the calculation for h^2_{cov}) is provided via the construction of independent distributions for h^2_X, h^2_Y, and r_p. These are specified as beta distributions because the latter is bounded between 0.00 and 1.00. The beta distributions for each component are specified independently of one another, and the user controls the shape and location of the distribution along the support region (i.e., between 0.00 and 1.00). The shape of the beta distribution for each of the parameters can be changed according to the researcher's prior information about the probable values for h^2_X, h^2_Y, and r_p. When the researcher is unsure what the probability distribution of a parameter should look like, he or she has the option to choose a uniform beta distribution (similar to the diffuse prior in Bayesian work; Gelman et al., 2014). Interested readers may consult the Appendix for further details on constructing the beta distribution(s) and for a general discussion of the estimation routine.

In most cases, including the current analysis, some information will exist regarding the heritability of a particular trait (Polderman et al., 2015). The development of the beta distributions for the current study is informed by prior research on the heritability of age at menarche (h^2_Y) and research on family structure (h^2_X) assessed in the form of having an absent father. The heritability estimates for both traits were assumed to range between 0.20 and 0.80 (although most estimates available from the literature were near 0.50; see Table 1) (Dick et al., 2001; Figueredo et al., 2004; Kirk et al., 2001; Mendle et al., 2006; 2009; Rowe, 2002; Towne et al., 2005; Trumbetta & Gottesman, 2000; van den Berg & Boonsma, 2006). Based on these findings, we set the distributions for h^2_Y and h^2_X to range between 0.10 and 0.90, but the majority of cases ranged between .40 and .60, with a mean and median of 0.50. The distribution for r_p was also constructed based on the published phenotypic correlations between father absence and

age at menarche. Drawing from evidence in the available literature (Table 1; Moffitt, Caspi, Belsky, & Silva, 1992; Surbey, 1990; Webster, Graber, Gesselman, Crosier, & Schember, 2014), the distribution for the phenotypic correlation (r_p) was set to range between 0.11 and 0.14.

As mentioned above, it is important to note that relatively little research is available regarding values for the genetic correlation (r_g) between these traits. We therefore opted to examine a range of values for r_g. The values for r_g used in this analysis ranged between 0.00 and 0.20. We chose this range of values for r_g because it is a conservative, yet realistic, range of values for the genetic correlation between our two focal variables. We start with values that indicate almost no genetic correlation between father absence and age at menarche (e.g., $r_g = 0.01$ and 0.02) and increase in increments of 0.01 up to 0.20. The latter value is, by most standards, only a small-to-moderate correlation, but it is one that likely represents the upper-limit for any genetic correlation between these two phenotypes. The logic of this argument is that there may be genetic components to both father absence and age at menarche, but only the latter (age at menarche) is likely to reflect a "direct" relationship with genetic factors. Any genetic influence(s) on father absence are likely mediated by a range of factors, each of which may serve to reduce the degree to which the genetic influence on father absence is correlated with the genetic influence on age at menarche.

3. Results

Having specified plausible values for the components of the simulation routine (see Table 1), the estimation tool was set to run $k = 10{,}000$ calculations, each time using a specified value for r_g (see below and Figure 2), and drawing a random value from the distribution for h^2_X, from the distribution of h^2_Y, and from the distribution of r_p (distributions presented in Figure 1). The values for r_g were set to range between 0.00 and 0.20. For example, consider $r_g = 0.05$. In this scenario, the value for r_g would always equal 0.05 and then 10,000 calculations would be carried out using random draws from the other three distributions to solve the equation for h^2_{cov}, resulting in a distribution of h^2_{cov} values. The results are presented in a series of 16 histogram plots provided in Figure 2. Each figure contains a blue vertical bar corresponding to the mean value of the estimates for h^2_{cov}. Additionally, each figure includes two green bars, which represent the location of the 95% credibility intervals.

The top row of Figure 2 displays the distribution of h^2_{cov} scores when r_g = 0.00, 0.01, 0.03, and 0.04 moving from left to right, respectively. These are very small values that would only emerge if the genetic overlap between *X* (father absence) and *Y* (age at menarche) was minimal. Even at these very small levels of genetic overlap, h^2_{cov} estimates are non-trivial. The mean and 95% credibility interval for each of these conditions is provided in Table 2. As expected, when r_g = 0.00, the mean for h^2_{cov} was 0.00, with no variance and a credibility interval that did not range beyond 0.00. This was a special test condition that was included to demonstrate that the tool works as it should: when *X* and *Y* do not share a genetic etiology (i.e., when r_g = 0.00), then h^2_{cov} should also be calculated as 0.00—as is the case in our model.

Of greater interest are the values of h^2_{cov} when r_g > 0.00. For example, when r_g = 0.01, the mean of h^2_{cov} was 0.05 with a 95% credibility interval ranging between 0.03 and 0.07. In other words, when the genetic correlation (r_g) between father absence and age at menarche is set to a low value (0.01), the percentage of the phenotypic correlation (r_p) that is attributable to a shared genetic etiology (i.e., the percentage of the correlation that is confounded by genetic influences) is about 5% with a probable range of values between 3% and 7%. Following this same logic, we can interpret the pattern of findings displayed in the remaining panels of Figure 2 and in the remaining portions of Table 2. As the genetic correlation (r_g) increases, the estimated degree to which the phenotypic correlation (r_p) is confounded with genetic influences (h^2_{cov}) also increases. Increasing to a genetic correlation (r_g) of 0.10, for instance, suggests that about 49% of the correlation between father absence and age at menarche (r_p) is explained by genetic factors, on average. In the final panel (bottom right of Figure 2), the genetic correlation (r_g) is set to 0.20. In this case, about 90% of the association between the two variables is the result of overlapping genetic factors (i.e., h^2_{cov} = 0.90, 95% credibility interval = 0.60 – 1.00). It is important to note that at genetic correlation (r_g) values of 0.14 and greater, the credibility interval in these cases all include 1.00. Put differently, one could logically expect that genetic factors *could* explain 100% of the correlation between father absence and age at menarche once r_g reaches 0.14.

4. Discussion

Certain methodological considerations have not been widely integrated into research designs testing human life history hypotheses. Among these methodological issues is the need to account for genetic confounding when examining the influence of specific familial environmental variables on life history traits. For research on father absence and age at menarche, specifically, this means that the non-zero heritability of both independent and dependent variables may confound the association between the two variables in observational studies (see Barnes et al., 2014).The current study used estimates available in the published literature (see Table 1) to inform a simulation model that estimated the extent to which the phenotypic association between father absence and age at menarche might be confounded by genetic variation.

Our results suggest that even a small genetic correlation between father absence and age at menarche could explain a sizable portion of the relationship between the two traits. For example, even moderately correlated genetic factors between father absence and age at menarche ($r_g \geq 0.14$) could almost completely confound the phenotypic correlations found in observational studies. At the conclusion of the simulations, with only a genetic correlation of $r_g = 0.20$ between the two traits, nearly the entire phenotypic correlation (90%) between father absence and age at menarche could be explained by genetic confounding. The results of the current research also provide a range of values demonstrating the extent to which genetic confounding occurs at various degrees of trait heritability and r_g—results that are not produced by classic empirical research designs.

What these results suggest is not that there is no environmental influence on age at menarche—approximately half the phenotypic variance in age at menarche is accounted for by environmental factors (Dick et al. 2001; Kirk et al., 2001; Rowe, 2002)—but that father absence specifically may not be the environmental input responsible for individual variation of menarche timing. The results of the current simulations corroborate research suggesting that the relationship between father absence and age at menarche may be spurious and confounded by genetic variation (D'Onofrio et al., 2006).

As noted previously, many genetically sensitive approaches—such as the differential sibling-exposure design (Tither & Ellis, 2008)—cannot fully account for genetic confounds, because siblings

only share approximately half of their genes. Classic twin designs that afford full control of genetic variation, however, show no significant influence of shared environmental effects on age at menarche (Dick et al. 2001; Kirk et al., 2001; Rowe, 2002), thereby raising questions about whether an ostensibly shared environmental factor (i.e., an absent father) could affect age at menarche (*cf.* Ellis, 2004). To the extent that genetic factors are correlated across phenotypes, it may explain, in part, the phenotypic association between father absence and age at menarche.

In a recent review regarding genetic confounding of reported phenotypic associations, Zietsch (2016) suggests, as do we, that controls for genetic confounding are necessary to secure a clear understanding of whether—and to what extent—the environment calibrates the development of life history strategies in the way that some evolutionary theorists have predicted (e.g., Belsky et al., 1991; Ellis, 2004). Prior research has already cast doubt on the predictive utility of father absence once genetic confounding is addressed (D'Onofrio et al. 2006; Mendle et al., 2006; 2009). The results of the current study illustrate the degree to which this may hold true under the conditions most likely to prevail in the population.

4.1. Implications for Human Life History

The current study focused on genetic confounding of the relationship between father absence and age at menarche, specifically. There are, however, a plethora of life history hypotheses that have been generated in light of Belsky et al.'s (1991) contention that early childhood environments calibrate life history outcomes, especially as these relate to the timing of pubertal maturation (Ellis, 2004). Implementation of research designs capable of disentangling the environmental and genetic influences on life history outcomes is limited (Dick et al., 2001; D'Onofrio et al., 2006; Ellis, Schlomer, Tilley, & Butler, 2012; Kirk et al., 2001; Mendle et al., 2006, 2009; Rowe, 2002 Tither & Ellis, 2008), and these research designs require substantial time and resources to execute. The current study highlights the utility of simulation modeling to estimate the extent to which genetic variation may confound phenotypic associations when genetically sensitive data are unavailable. Simulations, as used here, can profitably be applied to other life history hypotheses that have not yet been subject to rigorous, genetically sensitive

empirical study. The integration of behavioral genetic methodologies and life history research can generate important insights into human outcomes, including questions surrounding the sources of variation in life history traits. Results such as those generated in the current research can allow for greater refinement of human life history theory as the field of evolutionary psychology moves toward explicit integration of behavioral genetics into our theories.

The degree to which environmental experiences and genetic variation affect particular life history outcomes remains largely unclear, however. There also remain concerns surrounding the specific interplay of environmental experiences and genes (*r*GE, GxE) in producing life history outcomes. Environmental experiences do not, in all cases, manifest randomly without at least some input from the organism. Although certain factors are beyond manipulation by the organism (i.e., large-scale ecological shifts, famine, or natural disasters), social interactions, mate choice, and cooperation with other organisms, for example, are influenced directly by other factors, such as the personality traits and temperaments of the individual (Scarr, 1992). Organisms actively seek (active *r*GE) and evoke reactions from (evocative *r*GE) certain environments based on heritable traits (Kendler & Baker, 2007; Scarr & McCartney, 1989). Parents also endow offspring with an environment in which to live, and a genome comprised of half of each parent's genes. The mathematical consequence of this is that the environments children experience are correlated with the genotypes that they inherit from their parents (passive *r*GE) (Kendler & Baker, 2007).

Consider *r*GE as it relates to life history research investigating the effect of the familial environment on age at menarche. Age at menarche varies in the population due, in part, to genetic variation. Components of the environment that are hypothesized to influence pubertal maturation are not beyond the reach of genes. The type of parenting environment experienced by a child is moderately heritable (i.e., estimates around 0.40; Kendler & Baker, 2007), suggesting that studies examining outcomes such as age at menarche are subject to model misspecification if genetic and environmental sources of variance are not differentiated. If genetic influences cut across both the independent and

dependent variables—whatever they may be—then failure to account for the genetic correlation may distort estimates of the phenotypic association between the focal variables.

4.2. Limitations

The simulation strategy we employed in the current study provides an informed estimate of the extent to which the association between father absence and age at menarche may be confounded by uncontrolled genetic factors in the studies used to produce estimates for the phenotypic correlation between these two variables (i.e., r_p). The distributions presented in Figure 2, and the statistical values provided in Table 2, rest on the validity of the input distributions for the four parameters that are required to calculate h^2_{cov} (see Table 1). It is for this reason that we formed beta distributions for the various estimates in a way that would capture the most likely range of values for the h^2 of father absence, the h^2 of age at menarche, and the phenotypic (r_p) and genetic (r_g) correlations between these two variables.

Although simulations like ours are informative, they cannot replace empirically based research. Simulation designs rely on evidence secured from empirical work that directly estimates the parameters of interest after controlling for genetic confounding. Simulation techniques and empirical research can be used in tandem to understand human life histories. Simulation techniques, therefore, can be utilized in two important ways: (1) Once empirical evidence has accumulated, researchers can re-assess the body of literature concerning the potential causal association between environmental factors and life history outcomes, and (2) Simulation designs can be used as a barometer to estimate the extent to which specific environmental factors may calibrate life history outcomes prior to conducting rigorous genetically sensitive research designs. We encourage life history researchers to consider the points raised in this study and to estimate the correlation between father absence and age at menarche *after* controlling for genetic overlap between the two phenotypes.

Finally, the simulation routine used here is agnostic as to the direction of any causal influence between *X* and *Y*. We have argued that any genetic overlap between father absence and age at menarche will result in a (at least partially) spurious correlation between the two variables. Our arguments are

consistent with modern developments in life history theory and with the behavioral genetic concept of gene-environment correlation.

The simulations employed in the current study do not explicitly account for potential gene-by-environment interactions (GxE), or the interactions between age at menarche and other phenotypic traits. Any GxE that contributes to the correlation between father absence and age at menarche would be distributed in ways anticipated by the typical portioning of variance in behavioral genetic methodologies (see Purcell, 2002). In the domain of life history research, such GxE interactions are typically discussed in regard to differential susceptibility. Differential susceptibility theory posits that individual differences can result in individuals responding differently to the same environmental input (Belsky & Pluess, 2009), which would suggest that individuals may respond differently to father absence, consequently influencing age at menarche differently for some individuals. As mentioned in the Introduction, however, the *experience of an absent father* is not the same as *a father being absent* (see also, Plomin et al., 2013). Operationalization of father absence variables (and other hypothesized family environment variables) should more carefully be considered in future research. If the latter is being tested—a father being absent—for example, arguments in favor of differential susceptibility need to be explicitly tested, rather than used as arguments against evidence of genetic influences.

GxE interactions may explain, in part, why genetically sensitive designs often fail to find substantial effects of father absence on age at menarche, given that the GxE (e.g., the *experience* of an absent father) is not modeled (see 1.2. Genetic Influences on Pubertal Maturation in Girls; *cf.* Ellis, 2004). Research in the domain of personality psychology, however, suggests that although GxE interactions are potentially important for explaining psychological outcomes, moderation of the shared environment (an absent father constitutes an aspect of the shared environment), specifically, diminishes effects of genes only in extremely unusual (non-normative) circumstances (Krueger, South, Johnson, Iacono, 2008; see also, Harris 1995).

4.3. Conclusions

The research designs common in the field of behavior genetics offer tools for psychologists to refine their understanding of how evolutionary processes have shaped human outcomes (Penke, Denissen, & Miller, 2007). The statistical simulation tool presented here provides a mechanism for estimating the degree to which genetic confounding occurs between two variables when genetically informed data are not available. The current study focused on a prevalent hypothesis in the life history literature: that father absence is associated with earlier age at menarche (Belsky et al., 1991; Ellis, 2004). The results of our simulations revealed that even moderately correlated genetic factors between father absence and age at menarche could almost completely confound the phenotypic correlations reported in previous observational research in humans. The results accord with the results of previous studies (e.g., D'Onofrio et al., 2006) that have cast doubt on the father absence hypothesis. The findings of the current study provide a barometer for the degree to which previous and future life history studies risk genetic confounding. As a result, continuing to ignore genetic confounding in life history research may perpetuate findings that are unlikely to reflect the actual developmental processes operating within humans.

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Table 1. Input parameters for simulations

Age at Menarche		
h^2	Measure	Source
.50	Age at menarche	Kirk et al. (2001)
.40; .68	Pubertal development factor	Dick et al. (2001)
.44	Age at menarche	Rowe (2000)
.49	Age at menarche	Towne et al. (2005)
.30	Age at menarche	van den Berg et al. (2006)
Father Absence		
h^2	Measure	Source
.42	Pair-bonding	Trumbetta & Gottesman (2000)
.51	Paternal investment	Figueredo et al. (2004)
r_p of Father Absence and Age at Menarche		
r	Measure	Source
-.11	Rank order correlation between father absence and menarche	Moffitt et al. (1992)
-.12	Years father was absent and age at menarche	Moffitt et al. (1992)
.13	Years father was present and age at menarche	Surbey (1990)
.14	Years father was absent and age at menarche (meta-analysis)	Webster (2014)

Table 2. Mean and mode values, and 95% credibility intervals for h^2_{cov} estimates

	h^2_{cov}		
r_g	Mean	Mode	95% Credibility Interval
0.00	0.00	0.00	0.00 – 0.00
0.01	0.05	0.05	0.03 – 0.08
0.02	0.10	0.09	0.06 – 0.15
0.03	0.15	0.13	0.09 – 0.22
0.04	0.19	0.18	0.12 – 0.29
0.05	0.24	0.23	0.15 – 0.37
0.06	0.29	0.27	0.18 – 0.44
0.07	0.34	0.32	0.21 – 0.51
0.08	0.39	0.36	0.24 – 0.59
0.09	0.44	0.41	0.27 – 0.66
0.10	0.49	0.45	0.30 – 0.73
0.11	0.53	0.50	0.33 – 0.81
0.12	0.58	0.55	0.36 – 0.88
0.13	0.63	0.59	0.39 – 0.95
0.14	0.68	0.64	0.42 – 1.00
0.15	0.72	0.68	0.45 – 1.00
0.16	0.76	1.00	0.48 – 1.00
0.17	0.80	1.00	0.51 – 1.00
0.18	0.84	1.00	0.54 – 1.00
0.19	0.87	1.00	0.57 – 1.00
0.20	0.90	1.00	0.60 – 1.00

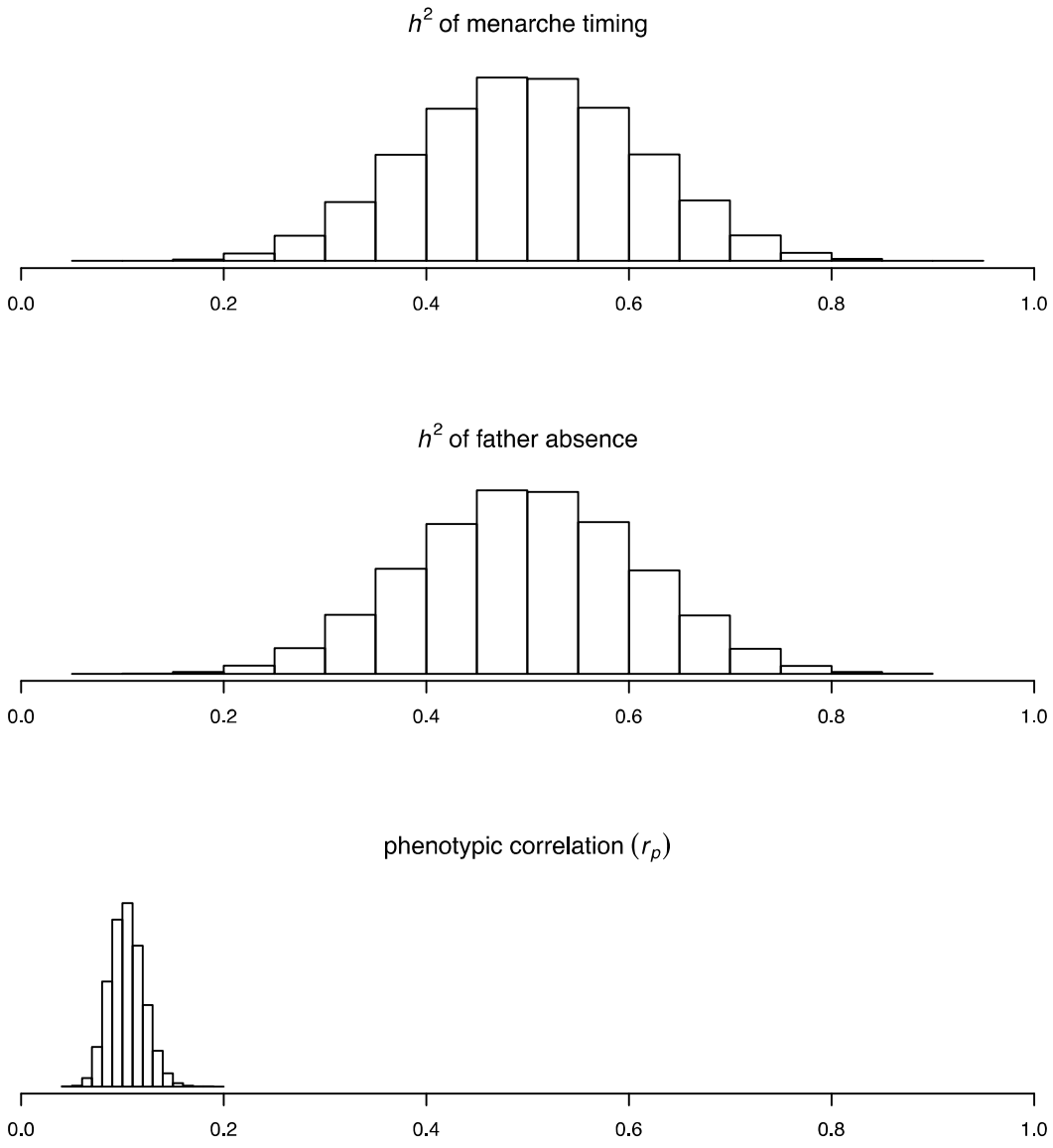

Figure 1. Probability Distributions for h^2_X, h^2_Y, and r_p

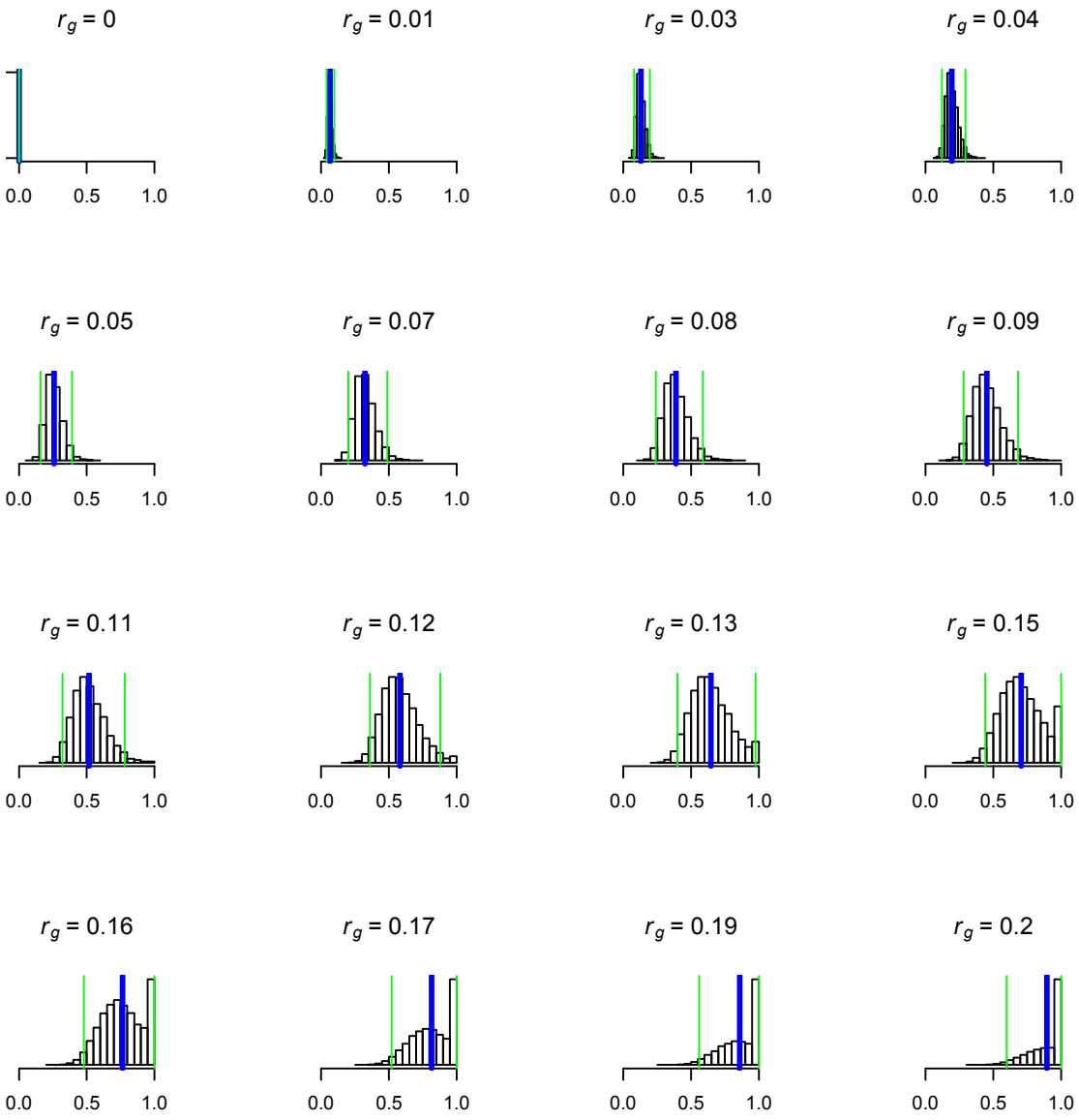

Figure 2. Distribution of h^2_{cov} at Different Values of r_g Blue (middle) bars represent mean values. Green (outer) bars represent 95% credibility intervals. See Table 2 for exact values.

Technical Appendix for: Genetic Confounding of the Relationship Between Father Absence and Age at Menarche

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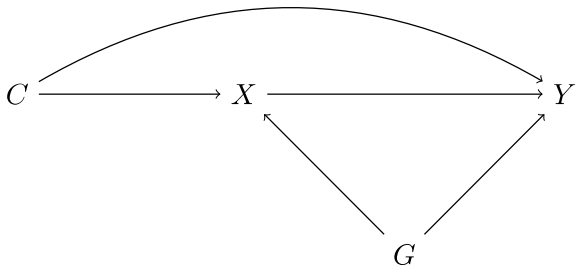
Imagine a researcher has a dataset with information on an outcome Y, a key independent variable X, and a host of covariates C, but s/he does not have a way to control for genetic factors G, as in the diagram below:



This sort of scenario presents itself in many—if not most—behavioral science studies. When this happens, scholars are forced to either: 1) abandon viable ideas for fear of producing biased parameter estimates; 2) expend more resources to collect additional data (e.g., identify and interview MZ twins) so that a genetically sensitive design can be used; or 3) publish potentially biased parameter estimates. The purpose of this discussion is to present a novel alternative.

Specifically, the new tool developed here blends a well-established equation for estimating the degree to which a phenotypic correlation r_p is driven by genetic correlation r_g with modern statistical simulation methods. By combining these two elements, one is able to simulate the degree to which an observed correlation may be sensitive to uncontrolled genetic influences. The degree to which r_p is sensitive to genetic influences will be referred to as h^2_{cov}. In the context of the above diagram, the tool developed here will allow one to estimate the degree to which the $X \rightarrow Y$ association (i.e., r_p) is sensitive to the inclusion of G.

In order to understand the estimation routine, it is first necessary to introduce the various pieces of information that must be supplied by the user. Then, the equation that sits at the center of the estimation routine—the equation for h^2_{cov}—will be introduced.

Necessary Information: r_p, h^2_X, h^2_Y, & r_g

The estimation routine is carried out in several steps. The first step is to estimate the phenotypic correlation between X and Y, referred to as r_p. This step can be carried out using any statistical analysis package and, it is worth pointing out, partial correlations can be used when available. In other words, there is no requirement that the unconditional correlation between X and Y be preferred over a partial correlation that has already accounted for other measured covariates C.

The second step is to arrive at an estimate for the heritability of X, h^2_X. Recognizing that this value is not directly estimable—because if it were, one of several other methods would be preferable to the present approach—the researcher is encouraged to consult the available behavioral genetic literature that has bearing on the heritability of the phenotype of focus (see Polderman et al. [2015] and/or the accompanying webpage: `http://match.ctglab.nl/#/home`).

The same is true for the heritability of Y, h^2_Y. While it is not necessary that the user be an expert in behavioral genetics, the utility of this novel tool is contingent upon the user inputting heritability estimates that are both meaningful and realistic.

We now have three pieces of information necessary for estimating h^2_{cov}, but in order to garner an estimate of h^2_{cov}, we will also need an estimate of the genetic correlation r_g between X and Y. In essence, r_g provides an estimate of the degree to which the genetic factors that affect X also impact Y. Thus, r_g is simply an estimate of the correlation between the genetic factors that influence the phenotypes—X and Y—of interest.

Building a Distribution of h^2_{cov} Estimates

Researchers interested in unpacking the covariance between X and Y often rely on one of several bivariate biometrical models (Loehlin, 1996). What is unique about the bivariate biometrical model is that the covariance between X and Y can be decomposed into a heritability component that we will refer to as h^2_{cov}. This value represents the proportion of the phenotypic correlation r_p that is due to a shared genetic overlap between X and Y.

One can calculate h^2_{cov} as:

$$h^2_{cov} = \frac{\sqrt{h^2_X} * r_g * \sqrt{h^2_Y}}{r_p}$$

where: $\sqrt{h^2_X}$ is the square root of h^2_X; $\sqrt{h^2_Y}$ is the square root of h^2_Y; r_g is the genetic correlation between X and Y; and r_p is the phenotypic correlation between X and Y. Conceptually, the equation provides an estimate of the proportion of r_p that is due to shared genetic influences between X and Y. For this reason, the equation for h^2_{cov} is the centerpiece of the new estimation tool developed here.

One might be tempted to simply solve for h^2_{cov} using estimates that come to mind for h^2_X, h^2_Y, r_p,

and r_g. Indeed, one can easily calculate the proportion of the phenotypic correlation that is due to genetic factors (i.e., h^2_{cov}) knowing nothing more than these four values. One key point, however, would be overlooked. Specifically, the inaccuracy of the estimates for h^2_X, h^2_Y, r_p, and r_g are ignored if one solves the equation with just one set of values. Of course, the very foundation of statistical analysis rests on the assumption of random error, meaning that any estimate we receive from this equation is likely to be too high or too low.

Fortunately, drawing on certain principles and techniques that have become commonplace in Bayesian analysis can help solve this problem. The mechanics of modern Bayesian statistical analysis is one of "brute force" sampling and simulation (Gelman et al., 2014; Gill, 2013; Jackman, 2000). Recognizing that integrating over the posterior distributions of interest—even for very simple problems—is often too complicated to calculate with closed form integral calculus, contemporary Bayesian statisticians have adopted Markov chain Monte Carlo (MCMC) routines of simulation and sampling as their primary workhorse for generating estimates of the posterior distribution. The logic is straightforward: if you cannot directly calculate a solution to a problem, use MCMC to simulate and estimate the problem a large number of times and create a distribution of posterior estimates.

Thus, the estimation tool developed herein will allow for the uncertainty of the estimates provided by the user to be taken into account when calculating the posterior distribution of h^2_{cov} estimates. This is done by solving the above equation k times, each time including a slightly different configuration of values for the heritability estimates and for r_p. The value k will be supplied by the user—it is recommended that k be set to a large value (e.g., $k = 10,000$) in order to ensure adequate coverage of the parameter space. Rather than force one to calculate the equation for h^2_{cov} for all the possible combinations of heritability estimates and r_p estimates—a procedure that would necessarily ignore the probability distributions of the various statistics—the approach developed herein allows one to randomly sample values from a distribution of heritability estimates and from a distribution of r_p estimates. But first, the user must construct said probability distributions. The beta distribution makes this task tractable.

The Beta Distribution

The beta distribution is appropriate for building a probability distribution of prior estimates for r_p and the heritability estimates because it is bounded at 0 and 1, but can take on any real value between those two integers. The beta distribution is a well-defined univariate distribution that has a direct relationship with the normal distribution and has a probability density function of (Gelman et al., 2014: 578; Leemis, 1986: 146):

$$f(x) = \frac{\Gamma(a+b)}{\Gamma(a)\Gamma(b)} * x^{a-1}(1-x)^{b-1}$$

where both a and b are greater than 0 and can be thought of as shape parameters that affect the form and location of the distribution along the support region. The three values of interest—the

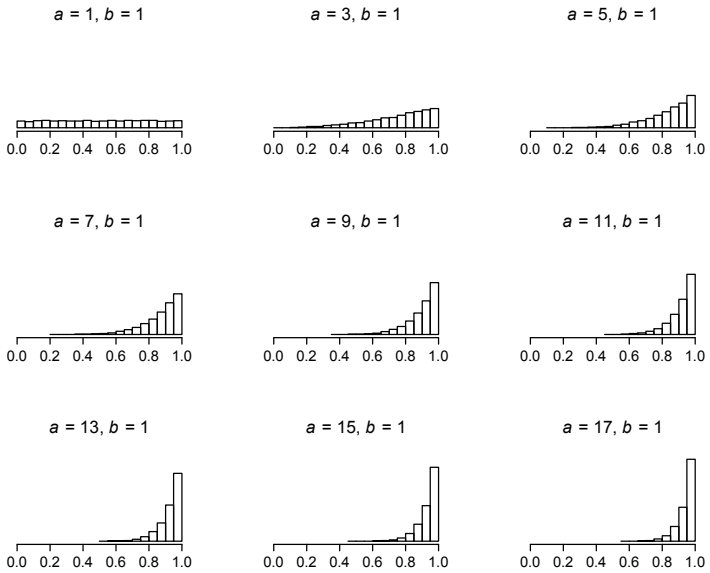
expected value [$\mathbb{E}(x)$], the mode [$mode(x)$], and the variance [$var(x)$]—are calculated as:

$$\mathbb{E}(x) = \frac{a}{a+b}$$
$$mode(x) = \frac{a-1}{(a-1)+(b-1)}$$
$$var(x) = \frac{ab}{(a+b)^2(a+b+1)}$$

Thus, the shape parameters can be used to adjust the balance point (i.e., the mean or expected value) of the distribution, the modal value, and the dispersion (i.e., variance) around the expected value. Generally, a can be thought of as the right shape parameter meaning that larger values for a, relative to b, will place more density in the right portion of the support region. The opposite is true for the shape parameter b, which is the left shape parameter. Taken together, this means that the user can adjust the beta distribution to load more density for the heritability estimate distribution and/or the r_p estimate distribution in the right side of the support region if a is increased relative to b and the opposite effect is achieved if b is increased relative to a.

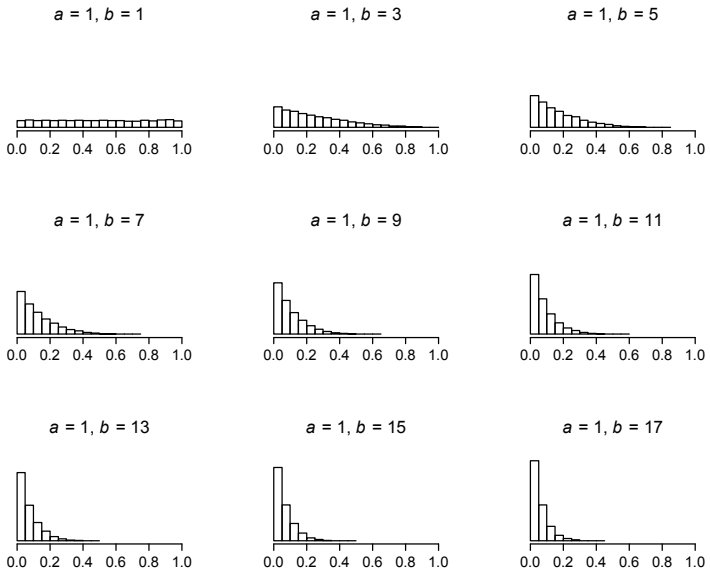
These points are demonstrated graphically in Figure 1 and Figure 2. Note also that the user can set the beta distribution to reflect his/her level of confidence in the estimates by setting the shape parameters to higher or lower values. Higher values for the shape parameters will load more density in increasingly smaller regions of the distribution, meaning the variance approaches its lower limit as a and b approach ∞.

Figure 1: The Effect of Changing a



Several other useful features of the beta distribution are worth pointing out. Imagine a scenario where the researcher is unsure what the heritability estimate(s) and/or the r_p estimate should be. In this case, the researcher would benefit from relying on something similar to the Bayesian diffuse/uninformative prior. This can be achieved by setting both shape parameters to equal 1 (i.e.,

Figure 2: The Effect of Changing b



$a = 1$ and $b = 1$). The panel in the top-left of Figure 1 and Figure 2 reveals the beta distribution is uniform under this condition.

Imagine another case where the researcher believes the heritability estimate(s) and/or the r_p estimate is approximately 0.50. This is an especially important value for the former (i.e., heritability estimates) because much of the behavioral genetic literature converges on heritability estimates that are approximately 0.50 (Polderman et al., 2015). These types of estimates can be modeled with the beta distribution by simultaneously increasing both shape parameters in equal magnitude (i.e., $a = b$). This relationship is revealed graphically in Figure 3.

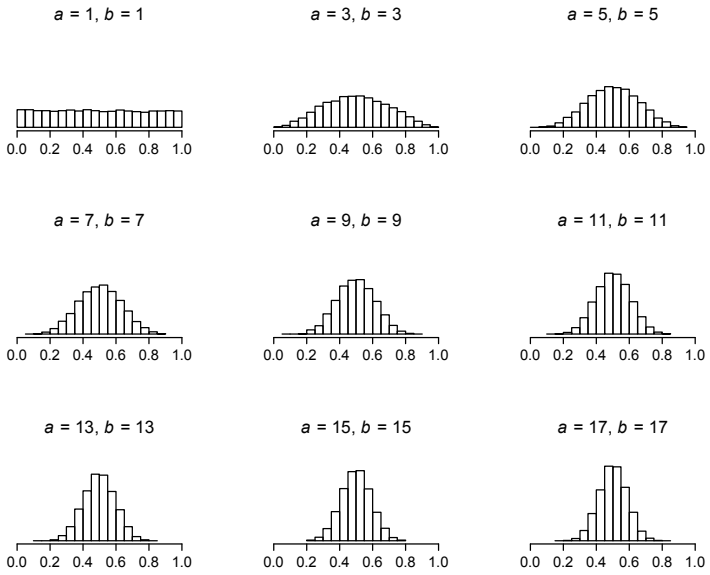
Recognizing that the true population parameter is an unknown that is only estimated in any given study, the beta distribution will capture the uncertainty in the estimates by building a range of values that will be fed through the equation for h^2_{cov} k times. In the end, a posterior distribution of estimates for h^2_{cov}—the degree to which r_p may be biased due to uncontrolled genetic influences—is retrieved.

Recommendations for Estimating a Distribution of h^2_{cov}

The above sections introduced a novel estimation tool that can be used by any researcher who is concerned that the relationship between two variables X and Y might be inflated due to uncontrolled genetic factors. All of the codes—in `R`—necessary to carry out the estimation routine have been posted to the following GitHub page: `https://github.com/jcbarnescrim`. Thus, access to genetically sensitive data is no longer necessary to estimate to extent to which a phenotypic correlation is sensitive to omitted genetic factors.

A brief summary of the estimation procedure is outlined here:

Figure 3: $a = b$



1. The researcher observes (whether from a novel data analysis or from the available literature) a relationship between two variables X and Y. The relationship should be measured in the form of a correlation coefficient (r_p), but note that a partial regression coefficient (i.e., an estimate that already accounts for other known confounders) can also be used as long as the value has been standardized.

    - Form a distribution of r_p values using the beta distribution. The expected value (or the mode if the distribution is skewed) of the beta distribution should be set to equal the observed correlation coefficient.

    - The shape parameters, a and b, are used to construct the desired beta distribution.

2. The researcher specifies the heritability estimate for X (h^2_X). This information should be based on the available behavioral genetic literature. Scholars are encouraged to see Polderman et al. (2015) for heritability estimates.

    - Form a distribution of h^2_X values using the beta distribution. The expected value (or the mode if the distribution is skewed) of the beta distribution should be set to equal h^2_X.

    - The shape parameters, a and b, are used to construct the desired beta distribution.

3. The researcher specifies the heritability estimate for Y (h^2_Y). This information should be based on the available behavioral genetic literature. Scholars are encouraged to see Polderman et al. (2015) for heritability estimates.

    - Form a distribution of h^2_Y values using the beta distribution. The expected value (or the mode if the distribution is skewed) of the beta distribution should be set to equal h^2_Y.

- The shape parameters, a and b, are used to construct the desired beta distribution.

4. The researcher specifies the genetic correlation between X and Y (r_g). This information may not always be available. In cases where r_g is unknown, the researcher is encouraged to try a range of potential values.

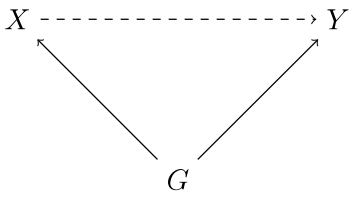
5. Enter the information from steps 1 through 4 into the program code located at (`https://github.com/jcbarnescrim`) and generate a posterior distribution of h^2_{cov} estimates. This distribution of estimates is calculated by feeding randomly drawn values from the above distributions through the equation for h^2_{cov} k times.

    - k is set by the user and should be a large value (e.g., 10,000) to ensure adequate coverage of the parameter space for the posterior distribution of h^2_{cov} estimates.

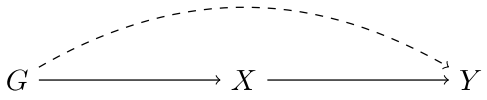
Conclusions

While there are many ways researchers could use this tool, the most obvious is to estimate the sensitivity of a parameter estimate of the association between X and Y (i.e., r_p). Rather than simply speculating about the degree to which a relationship might be confounded, a probability distribution of values can now be formed by carrying out the five simple steps outlined above.

But, it is important to caution researchers from blindly estimating a distribution of h^2_{cov} values. In fact, the distribution of h^2_{cov} values is only meaningful if genetic factors G serve as confounding influences. Confounding influences are those that are antecedent to X and Y and have a causal effect on variance in the two measures:



It is important to note, however, that confounding variables are statistically indistinguishable from mediator variables. This may complicate the interpretation of the results gleaned from the proposed tool if the true relationship is:



where X mediates the influence of G on Y. This chain of causation is quite different from that which is expected from a confounded relationship. Estimates of h^2_{cov} mean something different in this case, so researchers must rely on theory, empirical evidence, and logical deduction to determine whether the genetic correlation (i.e., r_g) between X and Y is due to genetic confounding or something else.

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