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## Human Mate Selection and Addiction: a Conceptual Critique

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### Abstract

The authors review past work on modeling human mate selection, and suggest, using illustrations from existing literature on the impact of alcoholism on relationship formation and dissolution and reproduction, that the challenges of adequately characterizing human mate selection have not yet been overcome. Some paths forwards are suggested.

### Keywords

mate selection; parental separation; reproductive timing

### Introduction

If a primary focus of behavioral genetic research is understanding the etiology of both normal human behavioral variation and psychiatric disorder, then the topic of human mate selection should be one central aspect. Perhaps the most important single action taken by an individual, in terms of its impact on the educational and physical and mental health outcomes of his/her future offspring, is the choice made of reproductive partner. Nearly one hundred years ago, Fisher (Fisher 1918; Fisher 1924) recognized that assumptions made about mate selection were critical for understanding how polygenic inheritance contributed to phenotypic correlations between relatives, and furthermore that different sets of assumptions might be made that would have differing implications for familial resemblance. A series of important publications by Eaves and colleagues in the late 1970s and early 1980s, as well as simultaneous work by other investigators (e.g. (Carey 1986; Cloninger et al. 1979; Rao et al. 1979)) reenergized theoretical work on this topic. In this conceptual review, honoring the contributions of Lindon Eaves, we will reconsider progress made in understanding human mate selection and its implications for the familial transmission of

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Editorial note

This paper was prepared for the Festschrift for Lindon J Eaves published in the May 2014 issue of this journal, but was inadvertently not included. We are happy to publish it now.

human behavioral variation and risk of psychiatric disorder. We will make efforts to follow the example set by Lindon Eaves, of honest and rigorous self-criticism with the goal of advancing the field of human behavior genetics. For purposes of illustration, we will draw primarily from examples concerning alcoholism and other addictive disorders, as examples of great public health significance which nonetheless capture well the complexities of modeling human mate selection. We will draw examples disproportionately from research studies by the various authors of this paper, since it would seem impertinent to be critical of others for short-comings apparent in our own efforts on this topic.

Consistent with the focus throughout his career, Eaves in his work on human mate selection emphasized modeling, hypothesis-testing, and identification of experimental designs that could advance knowledge. This work began with a clear statement of how failure to model the effects of human mate selection could lead to erroneous inferences about environmental causes of family resemblance, notably in the classical twin design (e.g. (Eaves 1977)): under phenotypic homogamy for a heritable trait, as originally derived by Fisher, c.f. (Bulmer 1980), the correlation between the additive genetic values of full sibs including DZ twin pairs would be greater than one-half; hence if such homogamy were ignored, this could lead to overestimation or even false-positive inference of family environmental contributions to variation. Most controversially, this led to a high profile publication on the inheritance of social attitudes (Martin et al. 1986) suggesting that, at least in Australia and the United Kingdom, once allowance was made for human mate selection, data were consistent with genetic rather than family environmental contributions to individual differences in attitudes.

Important extensions of this work came with the recognition that human mate selection was an inherently multivariate process (Eaves et al. 1984), and that there could be asymmetry by gender in the weighting of different traits for mate selection (Eaves and Heath 1981). This, if not correctly modeled, could for example mimic differing maternal versus paternal environmental influences in certain extended twin-family designs (e.g. twin pairs and their children). It is arguable that we still do not have a good understanding of the processes that lead to the observed joint multivariate distribution of the traits of biological mother and biological father pairs, nor therefore a good understanding of the implications of those processes for genetic and environmental risks in the offspring generation, nor even a good description of that joint multivariate distribution.

An additional important extension sprang from the insight that just as the classical twin design could be used, under strong simplifying assumptions, to decompose human variation into its genetic, shared and non-shared environmental sources (Eaves 1969; Eaves 1970; Jinks and Fulker 1970), similarly, by studying twin pairs and their reproductive partners (“spouses”: (Eaves 1979; Heath and Eaves 1985)), it should be possible to test hypotheses about the influences of heritable phenotype and of social background on human mate selection. Since different assumptions about mate selection would have different implications for the contributions of genetic and environmental transmission to family resemblance (e.g. (Cloninger et al. 1979; Heath et al. 1985; Rao et al. 1979)), it would be important either to test directly such competing hypotheses, or at minimum to conduct sensitivity analyses to examine the effects of misspecifying the assumed model for human mate selection.

## The Pastoral Era

We can best characterize this early work by Eaves and colleagues as describing an idyllic (hence pastoral) world. In contrast to the multitude of data-sets available for exploring the informativeness of classical twin pair and twins-plus-parents designs (e.g. (Eaves et al. 1978)), the relative lack of data for testing hypotheses about mate selection was undoubtedly a limiting factor. The early work on modeling human mate selection implies a world where all of reproductive age have partners, partners never change and partnerships never end; all reproduce successfully; and all children grow up with two parents. It implies a socially homogeneous world with none of the socioeconomic discontinuities (e.g. associated with secondary versus tertiary education) that may influence the probability that two individuals will become reproductive partners in ways not well captured by standard linear models. It assumes a world where all abide by the same rules of mate selection; a world where all family members cooperate in research; a world that can be adequately described by simple linear additive statistical models. In other words, this was a world of perpetual optimism, guided by the untested hope that slight deviations from these ideal conditions would not undermine inferences about human mate selection and the intergenerational transmission of genetic and environmental risks.

Donald Rubin (Rubin 1984) has commented that “it is generally not wise to obtain a very precise estimate of a drastically wrong quantity”. The field of behavior genetics has long recognized the trade-off between biased estimation and precision in its use of the classical twin design (comparing MZ and DZ twin pairs reared together) where, in the absence of separated twin pairs, there is strong negative confounding between non-additive genetic and shared environmental contributions to variation (Eaves 1969; Eaves 1970; Jinks and Fulker 1970). The assumption that non-additive genetic contributions to variation will be modest, and therefore in most cases ignorable – that the biases to estimated additive genetic, shared environmental and non-shared environmental variance components will be not too ‘drastic’ – seems to have been supported by the subsequent 40 years of research. Numerous applications of the classical twin design using large samples of twin pairs reared together have advanced our understanding of the critical role of genetic differences in creating behavioral differences between individuals. This progress would not have been possible if the field had relied upon the potentially less biased estimates achievable using the small numbers of extant separated twin pairs to supplement twin pairs reared together, thereby severely limiting the number and range of studies that could be conducted. It does not follow, however, that we can make strong simplifying assumptions in our idealized models of mate selection without rigorous analysis of whether we are in fact estimating drastically wrong quantities!

## Mate Selection in the Real World

Perhaps it is time for the field of behavior genetics to revisit the challenges of developing real-world research on human mate selection? The choice of reproductive partner would be expected to be profoundly important in shaping offspring talents, opportunities and behavioral and emotional problems. This is true from perspectives of both genetic inheritance and offspring environmental assets and risk-exposures. To simplify our task, we will ignore here mate selection in partnerships that never lead to reproduction or parenting,

while acknowledging that such partnerships may sometimes have important transient or even longer-lasting contributions to intra-generational variation in behavioral traits and psychiatric disorder risk (e.g. through marriage to or cohabitation with an abusive partner), and may also have consequences in delaying the formation of reproductive/parenting partnerships. This avoids the complication of how to classify non-reproductive partnerships in an era when a high proportion of cohabiting couples remain unmarried. We will also leave unexplored the complexities introduced by serial partnering and step-parenting: the challenges that we identify in characterizing human reproductive partner selection are only magnified in such cases.

The example of alcoholism illustrates some of the challenges of modeling human mate selection, seven of which we shall focus on here. We draw heavily here on our own studies on two adult twin cohorts from the Australian twin panel (Heath et al. 1997a; Knopik et al. 2004), and the partners of Australian cohort 1 twins (Grant et al. 2007), as well as on separate research on a US adolescent female twin cohort, who are being followed into their mid-30s (Slutske et al. 2004; Waldron et al. 2013). While adoption data emphasize the important role of genetic factors in the intergenerational transmission of alcoholism risk, the likelihood of selection against extreme high-risk families in the adoption process cautions against presuming the absence of important family environment influences (perhaps occurring in interaction with genetic differences) (Heath and Nelson 2002; Heath et al. 1997b). Classical twin study data are consistent with substantial heritability of alcoholism, variously defined (Heath et al. 1997b), with the caveat that any genotype x shared environment interaction effects are included in this estimate. Early data from treatment-ascertained alcoholics suggested strong assortative mating for alcoholism (Hall et al. 1983), and thus that alcoholism would be a useful ‘model’ for investigating assortative mating effects, and their implications for genetic and environmental transmission of risk. More recent work using general community samples is consistent with more modest but significant spousal concordance for alcoholism (Grant et al. 2007). Nonetheless, research on alcoholism has proved to be very fruitful in illustrating the challenges that we must face in research on human mate selection, and in identifying, in particular, the limitations to what can be inferred from cross-sectional data:

(i) Reproductive delay/infertility: Women (but not men) with a history of alcoholism, compared to non-alcoholics, show delayed reproduction (Waldron et al. 2008), despite the fact that women who are smokers tend to reproduce early (Waldron et al. 2009a) and that a high proportion of alcoholic women are smokers (Madden et al. 2000). Inferences drawn from cross-sectional studies are thus faced with the challenge of handling statistical censoring, that at any given age as yet unpartnered women will differ in important respects from those with partners. This particular challenge can be circumvented when we ascertain through children, focusing on partnerships that have successfully reproduced (Waldron et al. 2013).

(ii) Relationship breakdown: Alcoholics show both delayed marriage (for example, in data from an era when most reproduction occurred within marriage: (Waldron et al. 2011)) and accelerated relationship breakdown, with the chances of relationship breakdown especially high when both partners are alcoholic: in a US female adolescent twin cohort, where both

partners were necessarily together at least at the time of conception, using a broad measure of parental alcoholism (positive based on report of at least one informant), 77% of families with two alcoholic parents have experienced parental separation by twins' age 18, compared with 26% of families where neither parent was alcoholic (Waldron et al. 2013). Thus in cross-sectional samples, analysis of data from couples who are still together will disproportionately exclude couples who reproduced but were both alcoholic. Disproportionate loss of concordant affected couples will of course lead to a downward bias in the estimate of the reproductive partner correlation for alcoholism.

(iii) Participation bias: The challenge of detecting participation biases has long been recognized in research using the classical twin design (e.g. (Heath et al. 1998)). Alcoholism, smoking, separation from reproductive partner and low educational attainment are all significant predictors of reduced probability of research participation, although the predictors of non-response may vary as a function of the research focus (Dunne et al. 1997). Such biases are of course greatly exacerbated when using more elaborate research designs requiring data collection from more than two pedigree members (e.g. twin pairs plus spouses).

(iv) Reporting bias: The effects of participation bias can be somewhat mitigated by using family history reports obtained from cooperative family members (e.g. twin pair ratings of the alcoholism history of their partners: (Grant et al. 2007)), but only at the risk of introducing biases to estimates of mate selection parameters through any incorrectly modeled reporting biases. While there is generally good inter-informant agreement about parental history of alcoholism (Waldron et al. 2012), such biases might occur, for example, if a separated mother is more likely to acknowledge alcoholism in her ex-partner than a still married mother.

(v) Phenotypic convergence/divergence: In behavioral domains such as drinking, smoking and use of illicit substances, it is plausible that important reciprocal partner environmental influences will occur (e.g. (Grant et al. 2007; Heath 1987)). Although it is possible to imagine an ideal world in which partner similarity increases linearly with duration of cohabitation (often approximated in early work as duration of marriage, e.g. (Martin et al. 1986)), there are very little data to support this conjecture against the alternative possibility, that reciprocal influences disproportionately occur at the very early stages of a relationship. Under certain simplifying assumptions, it is possible to jointly model the contributions of mate selection and reciprocal mate environmental influences to the correlations between twin pairs and their partners (Grant et al. 2007), but with the caveat that misspecification of any part of the model will lead to biased estimates for the other model parameters as well.

(vi) Multiple factors determining partner choice: There are multiple factors that contribute to alcoholism risk, including personality variables (Slutske et al. 2002), other individual difference variables such as history of psychopathology and sociodemographic variables such as educational attainment or religious affiliation (Knopik et al. 2004), and family background factors that may include parental separation (Kendler et al. 1996) and childhood history of sexual or physical abuse (Dinwiddie et al. 2000; Kendler et al. 2000; Nelson et al. 2006; Nelson et al. 2002). Thus, while we may elect to focus on a single variable such as

alcoholism when attempting to model mate selection effects, we must do so in the knowledge that this simplification needs careful justification and attention to the biases that we may be introducing. It is indeed possible that partner concordance for alcoholism is entirely determined by ('secondary to') mate selection for other variables.

(vii) Linear additive model violations: In the specific context of genetic epidemiologic research on addiction, it is helpful to recognize that there are multiple components that jointly determine the development and course of a substance use disorder, including timing of first use (earlier first use predicts increased lifetime risk of disorder: (Grant and Dawson 1997)), patterning of use over time (e.g. total volume of alcohol consumed, frequency of heavy episodic drinking), dependence vulnerability conditional upon history of use (in other words, two individuals with very similar drinking histories may, for genetic or other reasons, have very different risks of dependence), and remission versus persistence of problems. These different components may show differential associations with the major risk factors identified by standard cross-sectional studies of addictive disorders, including of course differential influences by heritable factors and different patterns of gene-environment interaction effects; and their combined effects will likely not be well described in a simple linear additive modeling framework. This complexity applies *a fortiori* when we consider reproductive partner concordance for addictive disorders. To take one example, given the delayed reproductive relationship formation in alcoholic women, we should expect to find many in remission at the time of reproduction. Surely we would not expect alcoholics in remission, and those with active alcoholism, to partner with similar individuals, as implied by a standard linear model for assortative mating for alcoholism history. This suggests that we may even encounter a bimodal distribution for partner heaviness of alcohol consumption among female alcoholics, depending upon whether their relationship was formed at time of remission from symptoms, or during symptom persistence.

### Back to the Future

The seven challenges that we have identified above for modeling human mate selection suggest that complex sampling designs, when implemented using cross-sectional data-collection, can easily mislead us. If we simply implement a cross-sectional study of, say, twin pairs and any current partners, we have a reasonable chance of reaching conclusions that are drastically wrong. Developing elaborate multivariate models, built on inadequately tested assumptions, allowing for selection and reciprocal environmental influences, for participation biases and recall biases, and so on, is likely to further detain us in the world of pastoral. Several traditional research approaches however suggest simple ways in which we can begin to establish a firmer real-world knowledge base to guide efforts to model human mate selection and its implications for the etiology of behavioral variation and of psychiatric disorder risk. Here we focus on three approaches: (i) extending prospective cohort study designs to encompass information about reproductive partners; (ii) combining population data (e.g. derived from birth records or census data) and cohort study designs to take advantage of the power of the former (e.g. to describe the joint distribution of reproductive partners for educational level) and the ability of the latter to clarify the interpretation of population data; (iii) counterfactual (e.g. discordant twin pair) designs.

Cohort studies: Except in the case of small populations of uncertain generalizability (e.g. Iceland), the ideal goal of having prospective data on individuals who subsequently meet and ultimately become reproductive partners will not be achievable. Yet having at minimum prospective data on one of the partners, that predates relationship formation, provides some information about how partner characteristics may impact behavioral variation. This suggests that the obvious step of supplementing prospective behavioral genetic cohort studies – such as the traditional longitudinal twin studies – with collection of partner information will have value. There are many basic questions, for example, what are the baseline characteristics of an individual who partners with an alcoholic, or with a smoker, and how does that partnership impact the course of the individual's subsequent substance use, that can be addressed to move beyond the restrictive framework of simple cross-sectional univariate linear models.

Cohort-ecological approaches: The field of behavioral genetics has a long history of using population data-bases, e.g. comprised of birth records or national records or driver's license records, to ascertain informative samples. It is a small step from this to recognize that we can use such population data in their entirety to better characterize the structure of the human mating system, with considerable precision, with respect to key variables such as educational level or race and ethnicity. Such 'ecological' data come with their own challenges, notably the lack of detailed individual-level characteristics to inform interpretation, data missingness (e.g. births where the father is not identified) and the same issues such as censoring that apply in any cross-sectional data. They therefore become more useful when used in combination with prospective cohort study data, allowing the latter to inform interpretation of the former and vice versa.

Counterfactuals and mate selection: The importance of counterfactuals for causal inference has been implicitly recognized by behavioral geneticists and genetic epidemiologists for many decades, notably in the study of outcomes of exposure-discordant twin pairs that was an early motive underlying the development of Scandinavian twin registers. It received more general prominence in biostatistical work on causal inference in observational data led by Rubin, Rosenbaum and others (e.g. (Rosenbaum 2002; Rosenbaum 2010; Rosenbaum and Rubin 1983)). The central concept is that in theory the only way that we can with complete confidence infer a causal effect of exposure A compared to not-A is under the hypothetical condition where we can simultaneously observe outcomes in the same individuals under A and not-A conditions; the statistical challenge is to find approaches that most closely approximate this ideal, but impossible, experiment. In the biostatistical literature, these considerations have led to the development of propensity score methods and distance matching methods with the goal of achieving more robust causal inferences in observational data, inferences that are less critically dependent upon the strong assumptions of traditional linear additive regression or structural equation models (e.g. (Rosenbaum 2010)). These advances nonetheless have the important limitation that they have been developed for application to samples of unrelated individuals, and remain vulnerable to the effects of unmeasured confounders (e.g. unmeasured genetic influences common to both exposure and outcome measures).

In the behavioral and psychiatric genetic traditions, MZ twin pairs discordant for an environmental exposure (e.g. childhood sexual abuse) have been used to test for association with outcomes (e.g. adult psychopathology or addictive disorders: (Dinwiddie et al. 2000; Kendler et al. 2000; Nelson et al. 2006; Nelson et al. 2002)) with statistical control for some types of unmeasured confounders, namely those that show significant familiarity due to genetic or shared environmental influences (obviously, the problem of non-shared environmental confounders is not avoided). Often data from both MZ and DZ twin pairs are combined, based on post-hoc tests of homogeneity of conditional odds ratios as a function of zygosity. Consideration of such research in a counterfactual framework however reminds us of the limits to its generalizability: for example, childhood sexual abuse is being redefined in discordant twin-pair studies, to those cases where only one member of a twin pair was victimized, presumably therefore disproportionately excluding cases of familial sexual abuse.

Let us return to the fundamental question that we identified to motivate research on mate selection, namely understanding how reproductive partner choice impacts risks to offspring. This is a question that fits naturally in a counterfactual framework, for example, asking what is the impact (in terms of offspring behavioral and emotional outcomes) of a woman taking an alcoholic partner, rather than a non-alcoholic partner, taking into account her own characteristics. Both discordant-pair and between-family propensity score/matching methods would appear to have applicability in the generation of more robust approaches, not critically dependent upon linear additive models, to characterize human mate selection effects on risks in the offspring generation. The discordant pair approach might contrast outcomes in the offspring of MZ twin sisters discordant for reproduction with an alcoholic partner. In practice, this ignores the multiple traits on which the alcoholic partner of sister A differs from the non-alcoholic partner of sister B, in addition to the within-twin pair differences for those and other traits; as well as complications such as the differences in reproductive timing noted earlier that make such comparisons challenging. In other words, we are not at all close to the ideal counterfactual contrast of twin sisters with reproductive partners who differ ONLY in that one but not the other partner is alcoholic! In practice, therefore, it is likely that between-family matching methods, which can more closely approximate the counterfactual ideal, and can be implemented within a children-of-twins framework to provide partial control for unmeasured genetic confounders (e.g. (Jacob et al. 2003; Knopik et al. 2006)), will be more informative.

How might such an analysis proceed? While more elaborate matching methods could be implemented (e.g. using paired or one-to-N Mahalanobis distance matching: Rosenbaum, 2010), it is likely that a simple propensity score approach will generate important and clear insights. Following Rosenbaum and Rubin (1983), such an approach might develop a logistic regression model predicting partnering with an alcoholic (or a multinomial logit regression predicting a multiple-category addiction partner phenotype, e.g. alcoholic smoker, non-alcoholic smoker, non-smoker alcoholic with non-smoker non-alcoholics the reference group). Predictors would be characteristics of the twin that predate partnership formation, and might include family background variables (e.g. parental educational levels, parental alcoholism, parental separation, childhood physical and sexual abuse histories) and individual difference variables (psychiatric history that predates partnership formation;



educational level; personality variables, smoking and other lifestyle variables, etc.). Ultimate outcomes, contrasting offspring of those with alcoholic versus non-alcoholic partners, might be offspring alcohol or other substance use variables (c.f. (Jacob et al. 2003)), or internalizing or externalizing symptoms that are important predictors of later substance use involvement (c.f. (Knopik et al. 2006; Waldron et al. 2009b)). A critical point is that since it is the presence or absence of partner alcoholism history, stratified by the predicted probability of partnering with an alcoholic, that will be used to predict child outcomes, overfitting at the propensity score (logistic regression) modeling stage, with possible inclusion of multiple interaction or non-linear terms, is not problematic (see e.g. collected papers in (Rubin 2006)). Categorizing the predicted probability of partnering with an alcoholic into a relatively small number of categories (e.g. quintiles) will allow within-quintile contrast of the outcomes of the offspring in the case of alcoholic versus non-alcoholic partners with relatively little loss of precision (see Table 1), an insight that Rubin traces back ultimately to Cochran (Rubin 1984).

It is easy to see from the data-structure illustrated in Table 1 that a propensity score approach can lead to a number of instructive outcomes. The simplest is where the proportion of children with behavior problems is higher for women with an alcoholic partner than for those without, within every stratum. One alternative possibility would be that differences are seen only for intermediate and lower probability categories, implying that high-risk mothers will have an elevated risk of child behavior problems regardless of partner choice. Another alternative would be that zero cells would be found, e.g. that there would be essentially no women in the highest risk group with a non-alcoholic partner: an outcome perhaps unlikely for alcoholism, but more plausible for some traits for which there is very strong endogamy (e.g. religious affiliation or race in some cultures/groups). Such a finding would still be important, in showing that over part of the predicted probability range, no counterfactual cases exist, and no causal inferences can be made.

A current statistical limitation is that the statistical theory for propensity-score and matching methods has not been worked out for complex sampling schemes involving non-independent observations (e.g. twin pair data) (Rosenbaum 2002); but an approach using resampling schemes such as bootstrapping (Efron and Tibshirani 1993) could likely be implemented albeit at the cost of considerable tedium. Such between-family matching methods would be a natural extension to parallel the extension of twin cohort studies to encompass successive assessment of partners and then of the offspring-of-twins generation.

## Discussion

Developing better statistical models to account for human mate selection is an essential step towards the goal of improved understanding of the etiology of human behavioral variation and risk of psychiatric disorder. We have implied here that the first generation of linear additive models developed to describe human mate selection, formulated in an era of relative lack of data, may have become more of a hindrance than a help to progress. Modeling contemporary human mate selection requires a more comprehensive framework – for example, taking into account partner selection and deselection, delayed repartnering and delayed reproduction, participation bias and reporting bias – than the first ‘pastoral era’

models that were developed. It may turn out that the approximations used in those models are good enough, and do not seriously bias our understanding of how mate selection impacts genetic and environmental risks in the next generation. This may well prove to be the case for traits for which mate selection effects are rather weak, in which case the only costs of estimating elaborate linear models are the unnecessary diversion of time and intellectual effort. Given the fundamental importance of human mate selection as a determinant of genetic and environmental risks to the offspring generation, we as behavioral geneticists need to begin again the pursuit of rigorous understanding of human mate selection and its consequences.

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**Table 1**

Data structure for propensity score analyses contrasting child outcomes (e.g. proportion of children with behavior problems,  $x_{ij}$ ) for women who did or did not take an alcoholic reproductive partner <sup>a</sup>, stratified by predicted probability quintile estimated under a logistic regression model predicting having an alcoholic reproductive partner.

	Predicted probability of having an alcoholic reproductive partner <sup>a</sup>				
	Very Low	Low	Intermediate	High	Very High
Alcoholic partner	$X_{11}$	$X_{12}$	$X_{13}$	$X_{14}$	$X_{15}$
Non-alcoholic partner	$X_{21}$	$X_{22}$	$X_{23}$	$X_{24}$	$X_{25}$

<sup>a</sup>Estimated from logistic regression equation predicting reproductive partner alcoholism, and categorized into approximate quintiles.