Bias in Variance Components Due to Nonresponse in Twin Studies

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Incomplete data on trait values may bias estimates of genetic and environmental variance components obtained from twin analyses. If the nonresponse mechanism is 'ignorable' then methods such as full information maximum likelihood estimation will produce consistent variance component estimates. If, however, nonresponse is 'nonignorable', then the situation is more complicated. We demonstrate that a within-pair correlation of nonresponse, possibly different for monozygotic (MZ) and dizygotic (DZ) twins, may well be compatible with 'ignorability'. By means of Monte Carlo simulation, we assess the potential bias in variance component estimates for different types of nonresponse mechanisms. The simulation results guide the interpretation of analyses of data on perceptual speed from the Swedish Adoption/Twin Study of Aging. The results suggest that the dramatic decrease in genetic influences on perceptual speed observed after 13 years of follow-up is not attributable solely to dropout from the study, and thus support the hypothesis that genetic influences on some cognitive abilities decrease with age in late life.

The concept of 'nonresponse' refers to response values that are missing. In studies of behavioral traits, the nonresponse mechanism may reflect refusal, or inability to participate in the study. It is well known that nonresponse may bias results from behavioral–genetic analyses based on family data. Mathematical derivations, as well as simulations, have shown that selection (nonresponse) reduces the size of within-pair correlations (Martin & Wilson, 1982; Neale et al., 1989). Martin & Wilson (1982) showed that the reduction in estimated correlations depends on both the true correlation value and the selection mechanism, making a distinction between 'hard selection' and 'soft selection'. These earlier results clearly show that nonresponse may bias heritability estimates which rely on comparisons of monozygotic (MZ) and dizygotic (DZ) correlations. The effect of nonresponse on estimates of variance components in behavioral–genetic analyses has also been studied by means of simulation (Taylor, 2004). Taylor (2004) found that nonresponse primarily serves to attenuate the effect of shared environment and inflate estimates of nonshared environment and additive genetic effects.

The effect of nonresponse on variance component estimates depends on the estimation procedure used. Full information maximum likelihood (FIML), also referred to as raw maximum likelihood (e.g., Arbuckle, 1996; Lange et al., 1976), is the state-of-the-art procedure for estimation of structural equation models based on incomplete twin data, and is implemented in software packages such as Mx (Neale et al., 2003) and Mplus (Muthén & Muthén, 1998–2004). It allows the inclusion of both complete and incomplete twin pairs in the analysis. Alternative methods include multiple imputation (Rubin, 1987) and sample weighting based on the inverse of the predicted probabilities of response (e.g., Heath et al., 1998). The procedures mentioned above all produce consistent parameter estimates as long as the nonresponse is 'ignorable' (Little & Rubin, 2002).

The distinction between ignorable and nonignorable nonresponse is crucial to the discussion of the potential nonresponse bias. Therefore, we first give a definition of ignorable nonresponse based on probability models for twin data. Although the formal meaning of ignorable nonresponse is very clear once it has been defined, the potential effect of nonignorable nonresponse remains an issue in most empirical studies. The reason for this is that the assumption of ignorability cannot be checked based on empirical data.

Here we investigate how nonresponse may influence results from a classical twin analysis based on FIML. By means of Monte Carlo simulation we investigate how the nonresponse bias depends on the correlation between trait and liability to nonresponse. The simulations are based on a flexible nonresponse model similar to the model described by Neale and Eaves (1993), which is based on the idea that all individuals have an

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underlying liability to not respond. Liability to nonresponse is potentially influenced by both genetic and environmental factors, and these may be correlated with factors influencing the trait.

The twin model used in the simulations mimics the nonresponse pattern observed in a longitudinal study on Swedish twins, the Swedish Adoption/Twin Study of Aging (SATSA; Finkel & Pedersen, 2004). Nonresponse in SATSA is mainly due to loss to follow-up because of mortality or inability to continue to participate in the study. The longitudinal study design makes it possible to compare the sample characteristics for the group of participants that remain in the study with the group of participants that are lost to follow-up. However, as in any study where nonresponse is not part of the study design, the causes of nonresponse, and how these relate to the trait under study, are partially unknown. Therefore, dropout from SATSA serves as a good example of a nonresponse mechanism that may be nonignorable.

Longitudinal data from SATSA have been used to study the influence of genetic factors on the rate of change in cognitive function in old age. The issue of possible nonresponse bias has been raised but not formally addressed. Our simulations aim to shed light on the potential effect of dropout from the study. In initial analyses of perceptual speed, based on FIML, we found that the heritability estimates for perceptual speed decrease dramatically between the first test occasion and the fourth test occasion (after 13 years of follow up) of SATSA. This may be interpreted as support for the hypothesis that the relative importance of genetic influences on some cognitive abilities decrease with age in late life (e.g., Finkel & Pedersen, 2004). By means of Monte Carlo simulation, we study the potential effect of nonresponse on this interpretation. In the simulations we use the same trait heritability as observed for perceptual speed at the first test occasion of SATSA (Pedersen et al., 1992), and we mimic the rate of dropout up to the fourth test occasion.

Nonresponse in Twin Studies

Ignorable Versus Nonignorable Nonresponse

The distinction between ignorable and nonignorable nonresponse is best described by a probability model for the observed data. Let $\boldsymbol{Y}$ be the vector of trait values from one twin pair and let $P(\boldsymbol{Y}|\ \boldsymbol{X};\ \boldsymbol{\theta})$ be the probability model for $\boldsymbol{Y}$, where $\boldsymbol{X}$ denotes the covariates and $\boldsymbol{\theta}$ the model parameters. If some response values are missing we write $\boldsymbol{Y} = (\boldsymbol{Y}^{obs}, \boldsymbol{Y}^{mis})$, where $\boldsymbol{Y}^{obs}$ is the observed part, and $\boldsymbol{Y}^{mis}$ is the missing part. Let $\boldsymbol{R}$ be the vector of response indicators with elements equal to zero or one depending on whether the corresponding elements of $\boldsymbol{Y}$ are missing or observed. Nonresponse may depend on both trait values and covariates so a probability model for $\boldsymbol{R}$ can be expressed as $P(\boldsymbol{R}|\boldsymbol{Y},\ \boldsymbol{X};\ \boldsymbol{\xi})$, where $\boldsymbol{\xi}$ is the vector of model parameters. When some of the trait values are missing the 'observed data' truly consist not only of $\boldsymbol{Y}^{obs}$ but also of $\boldsymbol{R}$. The probability distribution of the observed data is obtained by integrating over the missing responses $\boldsymbol{Y}^{mis}$:

$$P(\boldsymbol{R},\ \boldsymbol{Y}^{obs}|\ \boldsymbol{X};\ \boldsymbol{\theta},\ \boldsymbol{\xi}) = \int P(\boldsymbol{R},\ \boldsymbol{Y}|\ \boldsymbol{X};\ \boldsymbol{\theta},\ \boldsymbol{\xi}) d\boldsymbol{Y}^{mis}$$
$$= \int P\ (\boldsymbol{R}|\ \boldsymbol{Y},\ \boldsymbol{X};\ \boldsymbol{\xi}) P(\boldsymbol{Y}|\ \boldsymbol{X};\ \boldsymbol{\theta}) d\boldsymbol{Y}^{mis}$$

One type of nonresponse is when data are *missing at random* (MAR), in which case $\boldsymbol{R}$ only depends on the observed part of the data, that is, $P(\boldsymbol{R}|\ \boldsymbol{Y},\ \boldsymbol{X};\ \boldsymbol{\xi}) = P(\boldsymbol{R}|\ \boldsymbol{Y}^{obs},\ \boldsymbol{X};\ \boldsymbol{\xi})$. For this type of nonresponse the joint probability distribution reduces to

$$P(\boldsymbol{R},\ \boldsymbol{Y}^{obs}|\ \boldsymbol{X};\ \boldsymbol{\theta},\ \boldsymbol{\xi}) = P(\boldsymbol{R}|\ \boldsymbol{Y}^{obs},\ \boldsymbol{X};\ \boldsymbol{\xi}) \int P(\boldsymbol{Y}|\ \boldsymbol{X};\ \boldsymbol{\theta}) d\boldsymbol{Y}^{mis}$$
$$= P(\boldsymbol{R}|\ \boldsymbol{Y}^{obs},\ \boldsymbol{X};\ \boldsymbol{\xi}) P(\boldsymbol{Y}^{obs}|\ \boldsymbol{X};\ \boldsymbol{\theta})$$

If the response values are MAR and the trait model parameters $\boldsymbol{\theta}$ and the nonresponse model parameters $\boldsymbol{\xi}$ are 'separable', the nonresponse is said to be *ignorable* (Little & Rubin, 2002). The parameters $\boldsymbol{\theta}$ and $\boldsymbol{\xi}$ are separable if the joint parameter space of $(\boldsymbol{\theta},\ \boldsymbol{\xi})$ is the product of the individual parameter spaces for $\boldsymbol{\theta}$ and $\boldsymbol{\xi}$, that is, if knowledge about $\boldsymbol{\theta}$ does not provide any information about $\boldsymbol{\xi}$ and vice-versa.

If the nonresponse is ignorable the estimation of $\boldsymbol{\theta}$ can be based on the likelihood ignoring the missing data mechanism, which is proportional to $P(\boldsymbol{Y}^{obs}|\ \boldsymbol{X};\ \boldsymbol{\theta})$. This likelihood function is the basis for FIML estimation, which is implemented in several structural equation modeling software packages. Thus, the procedures readily available for behavioral–genetic analyses assume that the nonresponse is ignorable. If the nonresponse is *nonignorable* a joint model for the trait values and the response indicators should be specified.

Ignorable Nonresponse in Twin Studies

For twin data, the response vector can be written as $\boldsymbol{Y} = (\boldsymbol{Y}_1,\ \boldsymbol{Y}_2)$, where $\boldsymbol{Y}_1$ and $\boldsymbol{Y}_2$ are the vectors of trait values for twin 1 and 2, respectively. Similarly, the vector of response indicators is partitioned as $\boldsymbol{R} = (\boldsymbol{R}_1,\ \boldsymbol{R}_2)$. Following the definition given in the previous section, the nonresponse is ignorable if the nonresponse model can be expressed as $P(\boldsymbol{R}_1,\ \boldsymbol{R}_2|\ \boldsymbol{Y}_1^{obs},\ \boldsymbol{Y}_2^{obs},\ \boldsymbol{X};\ \boldsymbol{\xi})$ and $\boldsymbol{\xi}$ and $\boldsymbol{\theta}$ are separable. An example of ignorable nonresponse is when $\boldsymbol{R}_1$ and $\boldsymbol{R}_2$ only depend on the observed responses $\boldsymbol{Y}_1^{obs}$ and $\boldsymbol{Y}_2^{obs}$, in which case the probability for a specific individual to drop out only depends on earlier observed response values. Another example of ignorable nonresponse is when $\boldsymbol{R}_1$ and $\boldsymbol{R}_2$ only depend on observed covariates, jointly denoted $\boldsymbol{X}$. For example, if the selection of participants is based on specific covariates, such as age and sex, and information about these covariates is available for all individuals the selection mechanism is ignorable.

If there is a within-pair correlation of nonresponse, possibly different for MZ and DZ twins, the nonresponse model can be expressed as $P(\boldsymbol{R}_1,\ \boldsymbol{R}_2|\ \boldsymbol{X};\ \boldsymbol{\xi})$, with $\boldsymbol{X}$ denoting zygosity. Hence, a within-pair correlation in nonresponse, possibly different for MZ and DZ twins, does not contradict the ignorability assumption per se. However, in this context it is

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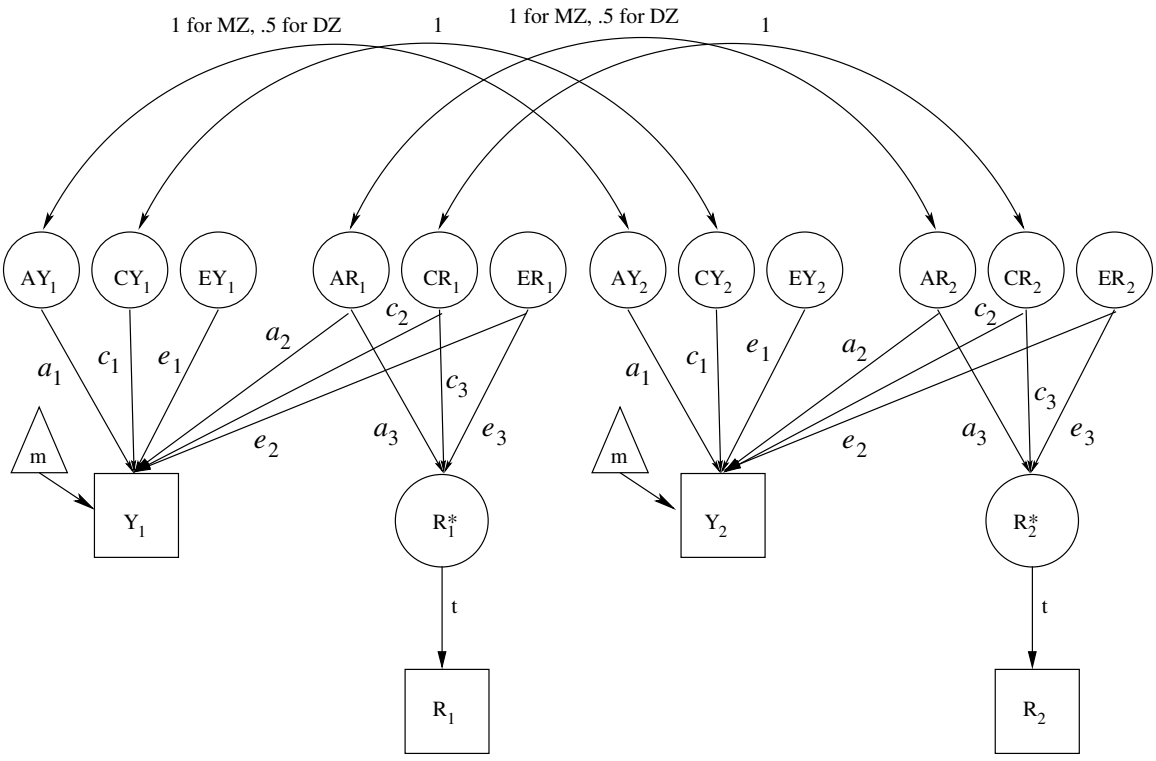

Figure 1

Path diagram on twin model for a univariate trait with nonignorable nonresponse.

important to note that the nonresponse will be nonignorable if $\boldsymbol{\xi}$ and $\boldsymbol{\theta}$ are nonseparable.

Nonignorable Nonresponse in Twin Studies

As an example of nonignorable nonresponse, consider a twin study on a univariate trait. A classical model for univariate twin data is the ACE model. The nonresponse indicator is a binary outcome: the trait value is either observed or missing. Hence, for each twin pair the vector of response indicators is a bivariate binary outcome, and can be modeled using the classical ACE liability model (e.g., Neale & Cardon, 1992). In this model, the response indicator R is equal to one or zero depending on whether the liability to nonresponse R^* lies above or below the threshold for being observed.

In our model, the genetic and environmental factors influencing liability to nonresponse are allowed to be correlated with the factors affecting the trait (Figure 1). We assume that many factors, or at least a moderate number of factors, are involved, and thus use a multivariate normal distribution for trait and liability to nonresponse (Kendler & Kidd, 1986).

The joint model for trait values and response indicators described by Figure 1 incorporates a wide range of nonresponse mechanisms. If the factor loadings a_2, c_2 and e_2, which describe the relation between trait and liability to nonresponse, are all equal to zero, the nonresponse mechanism is ignorable. In all other situations, some of the factors that influence the trait are related to factors that affect the liability to nonresponse, that is, they are in the pathway between trait and liability to nonresponse. If factors that are in the pathway between trait and liability to nonresponse are observed, the nonresponse is ignorable *conditional* on these factors. However, if the factors are unobserved they cannot be adjusted for in the model, and the nonresponse mechanism is nonignorable.

We make the standard assumption that all latent variables which correspond to genetic and environmental factors are independent and normally distributed with mean zero and variance one. The factor loadings are free to be estimated. The assumption of no gene × environment interaction, or gene–environment correlation, results in an additive expression for the genetic and environmental correlation components. Using the notation introduced in Figure 1, the correlation between trait value Y and liability to nonresponse R^* is

$$\rho = \mathrm{Cor}(Y, R^*) = \mathrm{Cov}(Y, R^*)/\sqrt{\mathrm{Var}(Y)}\sqrt{\mathrm{Var}(R^*)}$$
$$= (a_2a_3 + c_2c_3 + e_2e_3)/\sqrt{\mathrm{Var}(Y)} = \rho_A + \rho_C + \rho_E$$

where the third equality is due to the convention of setting the variance for the liability equal to one in liability models (e.g., Neale & Cardon, 1992).

The nonresponse bias in parameter estimates depends not only on the absolute value of the correlation between trait and liability to nonresponse, but also on whether it is genetic or environmental factors that induce this correlation. The correlation ρ

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between trait and liability to nonresponse is typically unknown in empirical studies. Although this is also true for the correlation components, ρ_A, ρ_C and ρ_E (also known as phenotypically standardized covariances), these are bounded by the trait etiology. For example, for a highly heritable trait the environmental correlation components have to be small as there are no influential environmental factors that can be in the pathway between trait and liability to nonresponse under this model. Consequently, the nonresponse bias has to be separately assessed for different trait etiologies. Here, we focus on the trait etiology observed for perceptual speed in a study of aging in late life.

Empirical Study

The SATSA Sample

The Swedish Adoption/Twin Study of Aging (SATSA) is a longitudinal twin study of aging that includes both questionnaire assessments and in-person testings of cognitive and functional capabilities, personality and health. It has been described in detail in Finkel and Pedersen (2004). The participants were identified via the Swedish Twin Registry (Lichtenstein et al., 2002; Pedersen et al., 2002). The first in-person testing (IPT1) took place between 1986 and 1988 and follow-up data were obtained after 3 (IPT2), 6 (IPT3) and 13 (IPT5) years. Testing took place in a location convenient to the twins, such as district nurses' offices, healthcare schools, and long-term care clinics.

We analyze data on perceptual speed measured by the Symbol Digit test (Pedersen et al., 1992). The sample is restricted to the 604 individuals (289 complete pairs and 26 incomplete pairs) with Symbol Digit scores from the first test occasion (IPT1) for whom zygosity is known (Table 1). Fifty-nine per cent of the sample are female, 64% are dizygotic and the average age at IPT1 is 64 years (range = 42–88). Of these 604 individuals, 441 participate in IPT2, 401 participate in IPT3, and 304 participate in IPT5 (due to funding considerations there was no in-person testing in the fourth 'IPT').

Table 1

Participants in SATSA With Scores on Perceptual Speed, Measured by the Symbol Digit Test

Occasion	IPT1	IPT2	IPT3	IPT5
MZ complete pairs	105	64	57	37
MZ incomplete pairs	6	25	28	27
DZ complete pairs	184	120	102	69
DZ incomplete pairs	20	48	55	65
Number of individuals	604	441	401	304
Missing individuals	—	27%	34%	50%

Statistical Analyses

The scores from the Symbol Digit test, expressed as percentage of maximum score, are separately analyzed for each test occasion. By fitting an ACE twin model to data from each test occasion an estimate of the heritability is obtained for each test occasion. The model estimation is based on FIML, allowing the inclusion of both complete and incomplete twin pairs. As a measure of uncertainty in the parameter estimates we use profile likelihood confidence intervals (Neale & Miller, 1997).

Results

The results from the analysis of perceptual speed in SATSA, measured by the Symbol Digit test, are given in Table 2. The mean score decreases from 38.8 (37.6–40.0) at the first test occasion to 32.1 (30.5–33.7) at the fourth test occasion. The estimates of genetic variance are approximately the same at IPT1 to IPT3, but dramatically smaller at IPT5. During the same period, estimates of the nonshared environment variance are relatively stable, and the shared environment variance estimates increase. This results in a dramatic decline in estimated heritability of perceptual speed from .67 (.44–.84) at IPT1 to .01 (0–.37) at IPT5.

The decline in genetic variance that we observe has been found for several domains of cognitive ability in earlier analyses of SATSA data (Finkel & Pedersen, 2004). The interpretation has been that the genetic importance for cognitive functioning in old age decreases with age, perhaps reflecting terminal decline in cognitive abilities: the twin similarity for cognitive abilities decreases as members of a twin pair begin to decline at slightly different times and at slightly different rates.

Table 2

Parameter Estimates for the ACE Model for Perceptual Speed, Measured by the Symbol Digit Test in SATSA

Parameter	IPT1	IPT2	IPT3	IPT5
m	38.8 (37.6–40.0)	37.2 (36.0–38.5)	36.5 (35.0–38.0)	32.1 (30.5–33.7)
a^2	98 (64–132)	58 (23–96)	86 (37–140)	1.8 (0–52)
c^2	18 (0–50)	40 (0–73)	41 (0–85)	95 (51–127)
e^2	31 (24–41)	29 (21–42)	36 (25–53)	45 (29–60)
Heritability	.67 (.44–.84)	.45 (.18–.75)	.53 (.23–.83)	.01 (0–.37)

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Simulation Study

Simulation Setup

The simulations aim to assess whether nonignorable nonresponse could, at least in part, explain the dramatic decrease in heritability at IPT5. They are based on the joint twin model for trait and nonresponse described in the path diagram in Figure 1. Trait values and response indicators for each twin pair are generated as follows:

1. *Fix* the total trait variance Var*(Y)* and the genetic and environmental variance components for the trait a^2, c^2 and e^2.
2. *Fix* the proportion of missing values p and the factor loadings for the liability to nonresponse a_3, c_3 and e_3.
3. *Fix* the desired correlation components ρ_A, ρ_C and ρ_E, which describe the correlation between trait and liability to nonresponse due to genetic and environmental factors.
4. *Calculate* the factor loadings a_2, c_2 and e_2 (which drive the correlations) from the expressions $\rho_A = a_2 a_3 \sqrt{\text{Var}(Y)}$, $\rho_C = c_2 c_3 / \sqrt{\text{Var}(Y)}$ and $\rho_E = e_2 e_3 / \sqrt{\text{Var}(Y)}$.
5. *Calculate* the factor loadings a_1, c_1 and e_1 from $a_1^2 + a_2^2 = a^2$, $c_1^2 + c_2^2 = c^2$ and $e_1^2 + e_2^2 = e^2$.
6. *Generate* genetic and environmental factors influencing the trait and liability to nonresponse from a multivariate normal distribution with mean zero and covariance structure given by Figure 1. The within-pair correlation between additive genetic factors is equal to 1 for MZ, and equal to .5 for DZ, twin pairs.
7. *Generate* trait values Y_1 and Y_2 and nonresponse liabilities R^*_1 and R^*_2 for each twin pair using the factor loadings from step 2, 4 and 5, and the genetic and environmental factors from step 6.
8. *Delete* trait values Y if the liability to nonresponse is below the threshold t, that is, if $R^* < t$. The threshold t is the pth quantile in a standard normal distribution, where p is the proportion of missing values fixed in step 2.

Each simulation is based on 500 simulated data sets, with a sample size of 4000 MZ and 4000 DZ twin pairs (before the deletion of values in step 8 above). The proportion of nonresponse was set to 50% in all simulations, which corresponds to the amount of missing responses in SATSA after 13 years of follow-up. As only complete pairs contribute to the estimation of variance components, the subsample used for the variance component estimation is even less than 50% of the sample size. The proportion of complete pairs is lower for DZ twins compared to MZ twins in our simulations, which is also the pattern observed in SATSA. Computations based on the bivariate normal distribution show that the probability for a pair to be complete is indeed lower for DZ than MZ twins for any heritable trait (Martin & Wilson, 1982).

In the simulations, two scenarios are investigated. In scenario 1, the factor loadings are chosen to mimic genetic and environmental variances observed for perceptual speed at the first test occasion of SATSA (Table 2). It corresponds to a trait heritability of .67. The relative importance of genetic and environmental factors for liability to nonresponse is assumed to be the same as for the trait, which enables the investigation of the case when the correlation between trait and liability to nonresponse is equal to one. An additional five correlations between trait and liability to nonresponse, evenly spaced between 0 and 1, are also investigated. Each correlation value between 0 and 1 can arise in several ways, depending on whether genetic factors and/or (shared or nonshared) environmental factors induce the correlation. For each value of the overall correlation ρ we investigate three different types of nonresponse mechanisms by varying the genetic and environmental correlation components ρ_A, ρ_C and ρ_E (Table 3). For each of the simulated data sets, estimates of mean and variance parameters in the ACE model are obtained from FIML estimation.

In scenario 2, the roles of genetic and nonshared environment are exchanged compared to the first scenario. This corresponds to a trait heritability of .12. In all other aspects the simulations are conducted in a similar way as the simulations of scenario 1 described above.

Simulation Results

The simulation results from scenario 1, based on a trait heritability of .67, are given in Table 3. The mean of variance component estimates are also displayed graphically in Figure 2. As expected, there was no nonresponse bias in the simulation on ignorable nonresponse, with zero correlation between trait and liability to nonresponse. For all other types of nonresponse, corresponding to nonignorable nonresponse, some variance component estimates were biased. Table 3 and Figure 2 reveal that the nonresponse bias does not only depend on how strongly the trait and the liability to nonresponse are correlated, but also on the underlying pathway. The general trend is that the underestimation of familial effects, that is, genetic and shared environmental variance components, increases with increasing correlation between the trait and liability to nonresponse. However, the severity of the bias for a specific value of the correlation between trait and liability to nonresponse depends on the type of nonresponse mechanism. The individual-specific variance is also underestimated for some types of nonresponse mechanisms. However, even for large values of the correlation between trait and liability to nonresponse, the individual-specific variance can still be unbiased.

Table 3 includes both mean and coverage (proportion of hits in the 95% confidence interval) for the factor loading estimates a, c and e (the square root of the variance components). Even if a parameter estimate

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Table 3

Simulations on Nonresponse With True Factor Loadings $a = 9.9$, $c = 4.2$ and $e = 5.6$ (Scenario 1)

Correlations				Estimates *a*		Estimates *c*		Estimates *e*	
ρ	ρ_A	ρ_C	ρ_E	Mean	Coverage[a]	Mean	Coverage[a]	Mean	Coverage[a]
0	.00	.00	.00	9.91	.94	4.09	.96	5.59	.93
.2	.20	.00	.00	9.75	.92	3.98	.98	5.60	.94
.2	.00	.12	.08	9.93	.95	3.66	.99	5.49	.80
.2	.00	.00	.20	10.1	.90	3.95	.98	4.95	0
.4	.40	.00	.00	9.34	.60	3.39	1	5.61	.95
.4	.07	.12	.21	9.98	.96	3.01	1	4.85	0
.4	.27	.05	.09	9.47	.73	3.47	.99	5.48	.75
.6	.60	.00	.00	8.61	.00	2.00	1	5.62	.95
.6	.27	.12	.21	9.24	.39	2.35	1	4.85	0
.6	.40	.07	.13	8.79	.02	2.76	1	5.35	.26
.8	.67	.00	.13	7.14	0	3.00	.74	5.33	.19
.8	.67	.12	.01	7.09	0	0.02	1	5.74	.69
.8	.47	.12	.21	8.05	0	1.05	.67	4.87	0
1	.67	.12	.21	5.76	0	0.01	.99	4.94	0

Note: [a] Hits in 95% confidence interval.

is biased, the coverage may still be good. The coverage for the genetic influence is satisfactory and close to .95 in all situations where there are no genetic factors in the pathway between trait and liability to nonresponse, that is, when $\rho_A = 0$. However, if genetic factors are in the pathway, that is, if the genetic correlation component ρ_A is large, the genetic influence estimate may be both severely biased and have very low coverage. The coverage is also close to .95 for the environmental influences as long as these

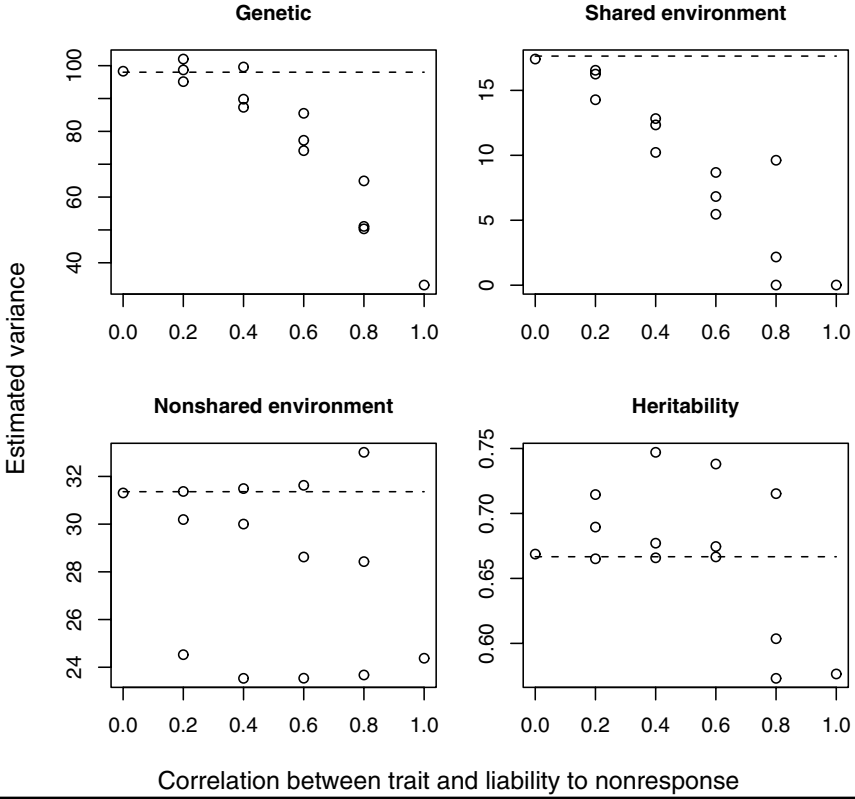

Figure 2

Means of estimated variance components and heritability for different values of the correlation between trait and liability to nonresponse for a trait with heritability .67 (scenario 1).

Note: Correct values are indicated with a dashed line (- - - -).

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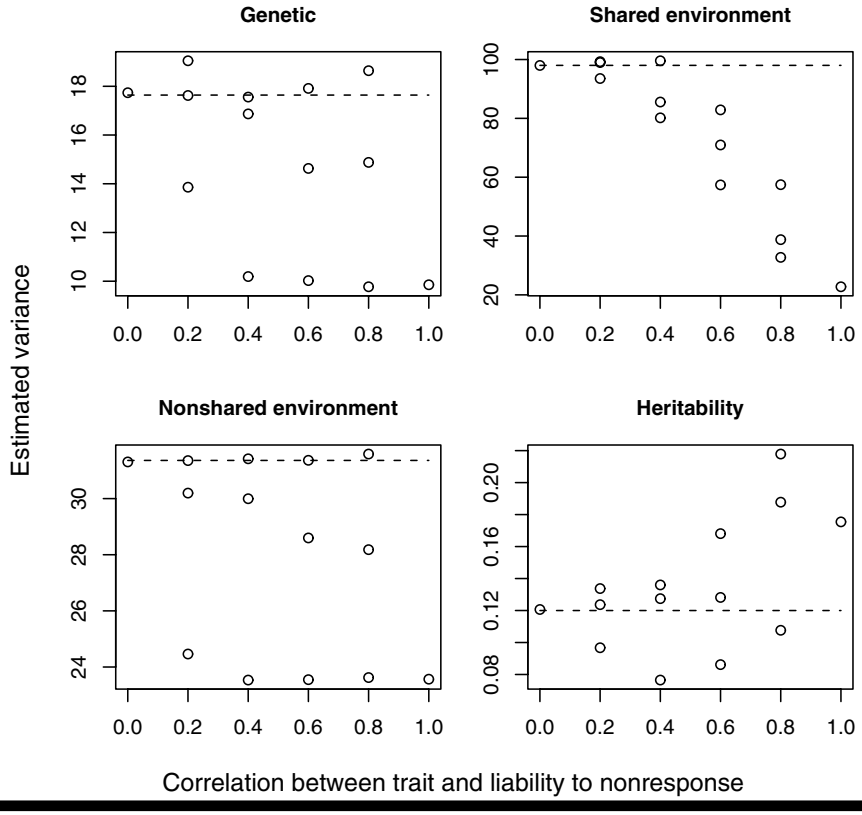

Figure 3

Means of estimated variance components and heritability for different values of the correlation between trait and liability to nonresponse for a trait with heritability .12 (scenario 2).

Note: Correct values are indicated with a dashed line (- - - -).

factors are not in the pathway between trait and liability to nonresponse.

The bounds on the correlation components have interesting consequences. With a trait heritability of .67 a high overall correlation between trait and liability to nonresponse can only arise if genetic factors contribute to it. Consequently, any conclusion about the magnitude of bias in estimates of genetic and environmental influences will depend on the relative importance of these factors. This is highlighted in Figure 3 showing the variance component estimates from simulations of scenario 2, with a true heritability of .12. Also here, the correlation between trait and liability to nonresponse mainly serves to attenuate all variance estimates. However, the correlation between trait and liability to nonresponse can be as high as .8, without a correlation between the genetic factors influencing trait and liability to nonresponse, and thus the genetic variance may remain unbiased.

We use the results from scenario 1 to discuss to what extent the decrease in genetic variance for perceptual speed observed in SATSA from the first test occasion to the fourth test occasion can be attributable to an effect of nonignorable dropout. In light of the simulations, the effect of dropout would be most severe if the liability to dropout is completely correlated with the trait mechanism. From Figure 2 we find that for a true genetic variance component of 98, the estimate can be expected to be as low as 33 in a situation with 50% dropout and a strong correlation between trait and liability to nonresponse. However, this is still larger than 1.8 which was observed at the fourth test occasion of SATSA. This suggests that the dramatic decrease in genetic variance for perceptual speed is not simply a nonresponse bias, and supports the hypothesis that the genetic influence on perceptual speed decreases with age in late life.

Discussion

We use a model for twin data that incorporates liability to nonresponse in order to assess the effect of nonresponse on variance component estimates. Several types of nonresponse mechanisms are considered. By means of Monte Carlo simulation we demonstrate that the bias in variance components estimates not only depends on how strongly the trait and the liability to nonresponse are correlated, but also on the underlying pathway. Therefore, there is no general answer to the question of how nonresponse in twin studies affects variance component estimates. This conclusion is in contrast to previous attempts to seek general answers as to how nonresponse influences variance component estimates (Taylor, 2004).

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Our model for liability to nonresponse extends the selection models considered by Martin and Wilson (1982) and Neale et al. (1989). The notion of 'hard selection' introduced by Martin and Wilson (1982), which means that the probability of selection is zero for individuals with liabilities below a fixed threshold value and unity for individuals above this value, is a special case of our model. It corresponds to the case where the correlation between trait and liability to nonresponse is equal to one. If the correlation is less than one, the nonresponse corresponds to 'soft selection'. However, in contrast to the models for soft selection presented by Martin and Wilson (1982) and Neale et al. (1989), we treat nonresponse as an outcome of its own, and use a flexible model for the underlying mechanism. Our model allows nonresponse to be influenced by both genetic and environmental factors. This makes it more flexible than the nonresponse model by Taylor (2004), which includes a correlation between trait and liability to nonresponse without considering different pathways between the two. Consequently, the finding of Taylor (2004), that is, that nonresponse primarily serves to attenuate the effect of shared environment and inflate estimates of nonshared environment and additive genetic effects, should not be interpreted as a generalizable result, it is completely driven by the choice of nonresponse model.

The joint model for nonresponse and trait data used in the simulations has some limitations. It assumes that there is no single factor that drives the nonresponse. Instead, a large number of independent factors, each with a small effect, are assumed to influence the liability to nonresponse. This is often a plausible assumption when incomplete participation is not part of the study design. The model also assumes that genetic and environmental factors are independent, which may not be true. If a gene × environment interaction is thought to be present, a more flexible model should be used. The general reasoning in this paper should be valid, though. Further, the model assumes that the factors acting on the trait and liability to nonresponse are positively correlated. Consequently, the nonresponse mainly serves to attenuate variance components.

As we have demonstrated, the main question is whether the nonresponse is ignorable. Based on the likelihood expression for twin data with incomplete information on trait values, we were able to show that a within-pair correlation of nonresponse, possibly different for MZ and DZ twins, is not by itself evidence of nonignorable nonresponse. If the nonresponse mechanism, possibly influenced by both genetic and environmental factors, is uncorrelated with the trait, estimates obtained from full information maximum likelihood methods are consistent and valid. This suggests that variance component estimates based on twin data with differential correlation in nonresponse for MZ and DZ twins need not always be mistrusted.

In some studies there may be reasons to expect that the liability to nonresponse among DZ twins is, on average, higher compared to MZ twins. For example, it may be that DZ twins are less enthused about twin research and consequently less willing to participate in a twin study. The bias this may induce depends on how a generally lower enthusiasm for twin research is related to the trait of interest. Although it is reasonable to believe that this relation is weak for most traits, there may be exceptions for measures of personality. If there may be a difference between MZ and DZ twins in mean trait level due to selection, this should be accounted for in the modeling stage by allowing MZ and DZ twins to have different mean parameters.

All external covariates related to the nonresponse should be included in the response model in order to get consistent estimates. Although the inclusion of external covariates is straightforward technically, it may introduce interpretational problems, as estimates of model parameters are *conditional* on all covariates in the model. For example, to assess the importance of genetic and environmental factors for the *overall variability* of a trait, a model without covariates should be used. On the other hand, if nonresponse is related to some covariates the MAR assumption is violated if these variables are excluded from the model. Consequently, in studies of a specific trait where nonresponse is known to be related to some other trait, a multivariate model for the two traits may be recommendable, even though the interest is only in one of the traits.

In studies of processes in late life, nonresponse due to mortality is often a reality. As many behavioral processes in late life are believed to be related to the time to death, nonresponse due to death is likely nonignorable, and has to be accounted for in the analysis. Therefore, models for longitudinal twin data that incorporate time to death have been proposed (Pedersen et al., 2003). It is also worth noting that trait values that are missing due to death are conceptually different from missing trait values where the participant is still alive. In the first case the values could not have been observed. If, however, both types of missingness are ignorable, the conceptual distinction between them does not affect the statistical treatment using FIML. However, nonignorable dropout due to death merits further investigation.

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