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Behavioral Genetic Approaches to Psychophysiological Data

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ABSTRACT

Behavioral genetic techniques have been developed to study the genetic and environmental contributions to individual differences in behavior, including covariances between different types of behaviors and stability of behaviors. Several studies have shown that certain psychophysiological characteristics appear to have heritable components. Therefore, it would seem appropriate that behavioral genetic techniques should be generalized for application to psychophysiological data. After reviewing general behavioral genetic methodology, this paper summarizes classical and new biometrical genetic techniques for both univariate and multivariate analyses, suggesting how these techniques are appropriate for the study of psychophysiological data and the relationship between psychophysiological variables and behavioral measures.

DESCRIPTORS: Classical genetic analysis, Biometrical approach, Twins, Adoptees, Siblings, Parent-offspring, Heritability, Environmentality, Additive effects, Dominance effects, Simultaneous estimation.

Individual differences in resting levels and responses to stimuli have been observed for all kinds of psychophysiological measures. The etiology of these differences may have important implications for future psychophysiological research. Behavioral genetic approaches to the study of individual differences, which involve estimation of the genetic and environmental contributions to observed differences in behavior, would seem to serve a useful role in the study of psychophysiological processes. The objective of the present paper is to describe the classical and more recent biometrical advances in behavioral genetic methodology as these can be applied to psychophysiological data. We begin by reviewing some of the studies which have demonstrated with traditional classical methods that psychophysiological data are influenced by genetic factors and are thus appropriate for the kind of analyses we describe. We then attempt to describe how biometrical methods can enhance understanding of the relative roles of genetic and environmental contributions to psychophysiological measures. Our discussion is not limited to univariate approaches; we also discuss how multivariate approaches (both classical and biometrical) can contribute to the understanding of psychophysiological processes.

The classical approach to behavioral genetics is a simple correlational method which involves measuring the similarity (correlation) of a behavior between individuals who are at a given level of genetic relationship (e.g., identical twins or unrelated pairs of individuals). This correlation is then compared to the correlation between individuals who are at different levels of genetic relatedness. Differences in similarity that correspond to differences in genetic relatedness are then interpreted as reflecting the genetic contribution to the behavior that has been examined. Biometrical techniques involve the the-

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oretical decomposition of interrelationships (i.e., into genetic and environmental components) and usually involve simultaneous estimation of maximum likelihood parameters. These techniques are also based upon comparisons of groups that are at different levels of genetic relatedness.

Both the simple correlational and the biometrical approaches can be used to investigate single psychophysiological variables or to study interrelationships of variables in a multivariate fashion. In the multivariate analyses, it is possible to examine the roles of genetic and environmental influences upon the interrelationships (covariances) among physiological variables. The same approach can provide estimates of genetic and environmental influences on covariance between psychophysiological variables and behavioral measures. Additionally, the multivariate approach can be used to study genetic and environmental contributions to psychophysiological variables taken repeatedly over time, thus providing estimates of the genetic and environmental factors that can contribute to the observed stability of the physiological measures.

Empirical Evidence for the Role of Genetic Factors

Because psychophysiological characteristics reflect biological processes, it is expected that some of these characteristics should be influenced by genetic factors. The empirical evidence supports this expectation, with much of the evidence from studies that obtained electroencephalogram (EEG) data, but with some from peripheral electrodermal research (skin conductance) and some from the study of cardiovascular activity (heart rate and blood pressure). In this section we shall review some of the evidence from research that has used the family design or the twin design. The review is not exhaustive, nor are these the only psychophysiological data that warrant genetical analyses. Our presentation is made for the purpose of demonstrating the level at which such analyses have been applied in the past and suggesting the appropriateness of more sophisticated analyses in the future.

EEG

A substantial number of studies have now concluded that genetic factors influence observed resting EEG patterns (see Davis & Davis, 1936; Juel-Nielsen & Harvald, 1958; Loomis, Harvey, & Hobart, 1936; Vogel, 1958; Young, Lader, & Fenton, 1972). Vogel has used the results of family studies to support his argument that the more closely related individuals tend to display "EEG variants" which appear to be distributed according to simple Mendelian modes of inheritance (Vogel, 1970, 1981). In a twin study Hume (1973) found higher identical twin than fraternal twin resemblances for average alpha frequency. Lykken, Tellegen, and Thorkelson (1974) and Lykken, Tellegen, and Iacono (1982) in their studies of twins have also found that some EEG characteristics appear to have a heritable basis but that the factors appear to be polygenic and that an epistatic effect (an interaction of several gene influences) is observed.

Genetic influence on evoked responses to visual stimuli has also been observed. Resemblances for identical twins compared to those for fraternal twins are consistent with an epistatic interaction, in that the fraternal twin correlations have tended to be near zero, whereas the identical twin correlations have been high (generally greater than .50). Results for auditory evoked potentials also suggest a genetic component in the response. Rust (1975) used biometrical methods described by Jinks and Fulker (1970) to find significant heritabilities using groups of twins. Surwillo (1980) confirmed this finding with a study of twins and unrelated pairs of individuals.

To our knowledge, no studies of heritability of EEG characteristics have used an adoption design. The results reported above are based on familial relatedness in intact families. Nevertheless, they support the hypothesis that genetic factors may have an important effect upon psychophysiological variables.

Electrodermal Activity

A similar pattern has been observed in the studies of skin conductance. A genetic component appears to be important in the development of response characteristics of the autonomic nervous system. Early work on the topic was completed by Jost and Sontag (1944), who studied autonomic response characteristics in identical twins, non-twin siblings, and pairs of unrelated individuals. Their finding that the identical twins were more similar than the other subject pairs suggests a genetic effect upon response characteristics. Rachman (1960) found that latency of the skin conductance response was significantly correlated within identical twin pairs. Lader and Wing (1966) provide evidence for genetic contributions to habituation of the skin conductance response. Hume (1973) observed more similarity within identical twin pairs than within fraternal twin pairs both for skin potential response to a stimulus and for habituation. Bell, Mednick, Gottesman, and Sergeant (1977) found identical twins in their sample to be significantly more similar than fraternal twins on measures of half-recovery time from responses and a measure of rise time to peak amplitude.

As with EEG analyses, none of the studies in this area has used an adoption design. The evidence suggests that some components of electrodermal activity in response to stimuli are genetically influenced. The methodology used in the electrodermal investigations, however, was not standardized across studies and was less than optimal for the purpose of generalization.

Cardiovascular Measures

Several twin studies have found evidence for genetic influence on heart rate level under resting conditions (Hume, 1973; Jost & Sontag, 1944; Lader & Wing, 1966; Mathers, Osborne, & DeGeorge, 1961; Shapiro, Nicotero, Sapira, & Scheib, 1968; Somsen, Boomsma, Orlebeke, & van der Molen, 1985). With respect to heart rate response (HRR) the findings have indicated that HRR under stressful conditions may be influenced by genetic factors (Vandenberg, Clark, & Samuels, 1965; Shapiro et al., 1968).

Two family studies (Hastrup, Light, & Obrist, 1982; Manuck & Proietti, 1982) have also suggested that HRR to stressful stimuli may be genetically mediated. The study by Hastrup et al. found that differences in HRR between sons of normotensive and sons of hypertensive parents were greatest under the most stressful conditions. A similar difference was seen for systolic but not for diastolic blood pressure. The Framingham family study (Havlik & Feinleib, 1982) observed that parent-offspring correlations for diastolic and for systolic blood pressure were of the same magnitude. Feinleib et al. (1977) report equally large heritability estimates for systolic and diastolic blood pressure based on twin data. Other twin studies (Mathers et al., 1961; Shapiro et al., 1968) also found evidence for genetic influence on blood pressure.

The Univariate Classical Approach

Intraclass Correlations and Estimates of Heritability

We have pointed out that many genetical analyses of psychophysiological measures have involved twin data. The classical approach to such investigation includes the calculation of intraclass correlations within genetically similar groups (e.g., identical or fraternal twins). Intraclass correlations (Haggard, 1958) reflect the percentage of the total variance on a measure that is observed between pairs of individuals (in analysis of variance terms, it is the ratio of the variance between twin pairs to the sum of the variance between and within pairs). Analysis of variance (ANOVA), in fact, is the way the estimates of variance are usually derived. Using this method for twin pairs, the intraclass correlation (t) is estimated as:

$$t = \frac{MS_B - MS_W}{MS_B + MS_W} \quad (1)$$

where MS_B and MS_W are the ANOVA derived estimates of between and within mean squares, respectively (Kirk, 1982). Significance of the correlation is given by the F-ratio of the ANOVA. The intraclass correlations, having been derived on each of the genetically similar groups, are then compared to one another to obtain an estimate of the relative role of the genetic influences.

If we assume that all of the variance that contributes to the similarity within pairs is due to genetic similarity and to shared environmental influences, and if we assume that the common environmental influences are the same for identical twins as they are for fraternal twins, then we can infer the extent to which the similarity of the measured characteristic is due to genetic influence. Stated formally, the intraclass correlation for identical twins (t_{MZ}) is the ratio of the covariance of the pairs of twins to the total variance observed in the sample of identical twins. The covariance of the pairs can be described as the sum of the covariance which is due to genetic influences (V_G) and that which is due to common (shared) environmental influences (V_{E_c}). It follows that $t_{MZ} = (V_G + V_{E_c})/V_t$, where V_t is the total variance. The intraclass correlation for fraternal twins (t_{DZ}) should differ from t_{MZ} only in the covariance that is genetically influenced (we have assumed that V_t and V_{E_c} are equivalent for identical twins and for fraternal twins). In fact, because fraternal twins share, on average, only half of their genes, genetic factors can contribute at most only half as much to the covariance of fraternal twin pairs. If we assume that the genetic covariance contributed to the similarity of fraternal twins is half that for identical twins, we can derive an estimate of the maximum heritability associated with the measured characteristic. Under this model, $t_{DZ} = (0.5\ V_G + V_{E_c})/V_t$. Thus, doubling the difference between the intraclass correlations for the identical and fraternal twins yields an estimate of the upper bound of broad sense heritability (Falconer, 1981):

$$h^2 = V_G/V_t \quad (2)$$

This is the proportion of the variance in the characteristic which is due to genetic variation. This upper bound estimate of heritability is accurate when only one genetic influence is present or, if more than one influence is involved, when the influences act in an additive manner. If dominance is involved or if polygenic influences are present and interact with one another, then the estimate will be biased upward. If the kind of genetic influence is known,

it is possible to correct for the bias in order to obtain a more accurate estimate of heritability.

An Example

To illustrate the classical approach, we present analyses of heart rate (HR) data obtained from Professor Robert Plomin of the Institute for Behavioral Genetics at the University of Colorado in Boulder. The sample consists of 58 twin pairs of children varying between 5 and 12 yrs. One measure recorded by Professor Plomin was HR level under resting conditions. Using these data we attempted to estimate the heritability of the measure. Standardized residual HR level (controlling for sex and age) was first calculated. We then completed ANOVA on the residuals, separately for the identical and fraternal twin groups. The results are presented in Table 1. Also reported in Table 1 are the intraclass correlations derived from the estimated mean squares by using Equation 1. In this way, we can estimate the HR level heritability to be $2(.533-.347) = .372$. About 37% of the variation in HR level is due to simple genetic influence.

Repeated Measurements

Most psychophysiological research involves the analysis of repeated measures. R.S. Wilson has published a series of papers on the analysis of repeated measures taken in twin studies (Wilson, 1968, 1975, 1978). The basic model of the analysis he employed is described by Winer (1962, p. 302 ff.), where it is classified as a two-factor mixed design with repeated measures on one factor (the psychophysiological variable) and each twin pair is considered as a group for the other factor. The method yields estimates of the correlation within twin pairs for the aggregate of the repeated measures and correlations within twin pairs for the morphology of the response curve. According to Wilson (1975) a repeated measures ANOVA used with Box's epsilon correction factor for twin data is more powerful than the alternative method of analyzing these data, a multivariate analysis of variance (MANOVA). Somsen et al. (1985) have used Wilson's methods to study phasic cardiac response morphology. They observed that genetic factors appear to have an influence under stressful conditions.

The Multivariate Classical Approach

Basis

We have discussed how it is possible to describe the variance of a psychophysiological characteristic in terms of the environmental and genetic components. There may be times when the psychophysiologist wishes to examine more than one characteristic. He or she might want to explore the genetic and environmental contributions to a correlation between variables. For instance, knowing the genetic contribution to the correlation between basal skin conductance level and average EEG frequency might make an important contribution to understanding the relationship between the two psychophysiological measures. Or, one might want to investigate the genetic or environmental contributions to the etiology of a relationship between a physiological measure (such as HR response) and a behavioral measure (such as shyness). In these instances, it is necessary to estimate the genetic and environmental contribution to the observed correlations between the variables.

One approach to this kind of analysis is the cross-correlational approach (Plomin & DeFries, 1979, 1981). Cross-correlations between a given characteristic (such as HR response) in one member of a twin pair and another characteristic (such as shyness) in the other member of the twin pair are used to decompose the observed (phenotypic) relationship into genetic and environmental contributions.

As Plomin and DeFries (1979, 1981) have stated, the observed correlation between the factors X and Y (where X could be HR response and Y could be shyness) is formally described as:

$$r_{P_xP_y} = h_x h_y r_G + e_x e_y r_E \qquad (3)$$

where $r_{P_xP_y}$ is the observed correlation between the characteristics X and Y, h_x and h_y are the root heritabilities of the individual characteristics (Equation 2), r_G is the genetic correlation (i.e., a measure of the extent to which two characteristics are influenced by the same genes); e_x and e_y are the root environmentalities of the variables (the proportion of the observed variance of each characteristic which is due to environmental causes: $e_x^2 = 1 - h_x^2$), and r_E is the environmental correlation (i.e., a measure of the extent to which two characteristics are affected by the same environmental influences.

Table 1

Mean squares and intraclass correlations for HR level

Twin Groups	MS Between	MS Within	MS Total	*F* Ratio	N	*p*	*t*
Identical	180.453	54.941	116.635	3.28	30	.0009	.533
Fraternal	145.214	70.473	107.154	2.06	28	.032	.347

Plomin and DeFries (1979, 1981) also point out that the cross-correlation between co-twins for the same characteristic (X = Y) is the same as the intraclass correlation for a single characteristic. When the characteristics are different the cross-correlation is precisely the definition of a correlation:

$$r_{P_xP_y} = \frac{\text{Cov } P_xP_y}{\sigma_{P_x}\,\sigma_{P_y}} \quad (4)$$

where Cov P_xP_y is the observed covariance of the characteristics X and Y, and σ_{P_x} and σ_{P_y} are the standard deviations of the observed characteristics. The cross-correlation for identical twins is stated as:

$$r_{P_xP_y} = \frac{(\text{Cov } G_xG_y + \text{Cov } E_xE_y)}{\sigma_{P_x}\,\sigma_{P_y}} \quad (5)$$

where Cov G_xG_y is the component of the observed covariance between X and Y that is due to genetic influences and Cov E_xE_y is the component of the observed covariance between X and Y that is due to common environmental influences. This follows because:

$$\text{Cov } P_xP_y = \text{Cov } G_xG_y + \text{Cov } E_xE_y \quad (6)$$

for identical twins (as long as gene-environment interactions can be ignored). When all of the genetic influence is additive, the genetic covariance for fraternal twins is, on the average, half that for identical twins; when dominance or polygenic interaction effects are present, the contribution of the genetic covariance to the observed covariance for fraternal twins will be less than half that for identical twins. Therefore, for fraternal twins:

$$r_{P_xP_y} \leq \frac{(0.5 \text{ Cov } G_xG_y + \text{Cov } E_xE_y)}{\sigma_{P_x}\,\sigma_{P_y}} \quad (7)$$

As described by Plomin and DeFries (1979, 1981), doubling the difference between the identical and fraternal twin cross-correlations (Equations 5 and 7) provides an estimate of the genetic contribution to the phenotypic covariance between traits X and Y when all of the genetic influence is additive:

$$\frac{\text{Cov } G_xG_y}{\sigma_{P_x}\,\sigma_{P_y}} = \frac{\text{Cov } G_xG_y}{\sigma_{G_x}\,\sigma_{G_y}} \cdot \frac{\sigma_{G_x}}{\sigma_{P_x}} \cdot \frac{\sigma_{G_y}}{\sigma_{P_y}} = r_G h_x h_y \quad (8)$$

When some of the influence is due to dominance or epistatic effects, $r_G h_x h_y$ will be overestimated.

Because we can derive h_x and h_y using univariate analyses (Equation 2), we can estimate r_G. By subtracting $r_G h_x h_y$ from the phenotypic correlation, we obtain $e_x e_y r_E$; then, by using the environmentalities derived from univariate analyses, we can also derive r_E.

An Example

Looking again at Professor Plomin's data, we found a significant correlation between HR responses recorded under two stimulus conditions: $r_{P_xP_y} = .795$; $p < .001$. The cross-correlation for MZ twins in the sample was .60; for the DZ twins it was .36. Doubling the difference provides an upper bound estimate of the genetic contribution to the phenotypic covariance between the two response measures (HRR1 and HRR2): $r_G h_x h_y = .48$. The heritability (h^2) for HRR1 was .60, for HRR2 it was .46. In this case, the genetic correlation (r_G) is .92, which means that both HR responses are to a large extent influenced by common genetic factors. (However, note that these genetic factors only account for about half of the variance in both task conditions.) The environmental correlation (r_E) can be estimated to be .68 and reflects the extent to which both responses are influenced by the same environmental factors.

Additional Points

Two additional points are relevant to the classical multivariate approach. One of these is that the two characteristics under study (X and Y) do not have to be different characteristics. They can be the same characteristic measured at two time points. In this instance, the question addressed involves the genetic and environmental contributions to the stability of the measure. For instance, the relationship between relative Beta EEG power at age 12 might be examined in relation to the same measure at age 22. The stability of the relative activity in the Beta band could be due to environmental stability over time or to genetic influences. The proposed analyses would estimate the extent to which each of these influences is involved.

The other relevant point is that the design does not require individuals under study to be twins. As long as the genetic relationships of the subjects are known, it is possible to compare two differently related groups. For instance, biological mother and offspring could comprise one group, and adoptive mother and adoptee might form another. No genes would be shared by the adoptee and adoptive mother, whereas the biological mother and child would have half of their genes in common. These relationships can be substituted as appropriate and the univariate or bivariate analyses described above can be performed.

Univariate Biometrical Analyses

Introduction

The classical approaches to the analysis of data for genetic and environmental contributions involve the comparison of two groups of subjects who are at different levels of genetic relatedness. One advantage of biometrical methods is that several groups of subjects at different levels of relatedness

can be studied simultaneously. For example, pairs of unrelated individuals adopted into the same home and reared together can be studied along with identical and fraternal twins and pairs of non-twin siblings. Using these four groups would permit simultaneous estimation of the extent to which the genetic influence is additive, the contribution of dominance or epistatic influences, the importance of common sibling environmental influences, and the contribution of unique environmental influences.

Simple Path Model

The path model presented in Figure 1 depicts the basic theoretical decomposition of the genetic (G), common environmental (E_c), and separate environmental (E_s) influences upon observed (or phenotypic) behavior (P) as described by Plomin, DeFries, and McClearn (1980). Similarity due to genetic influence upon the behavior of the pairs of subjects varies as a function of the extent to which the pairs are related ($r_{G_1G_2}$). For fraternal twins, the genetic correlation is between 0.5 and 0.0, depending upon the extent to which dominance and epistatic influences are involved (Falconer, 1981). The magnitude of the genetic correlation for biologically unrelated individuals reared together obviously is 0.0, as they have no genes in common. For identical twins the correlation is 1.0.

Decomposing the Model

The formal model presented in Figure 1 depicts the underlying factors that may account for behavioral similarity or dissimilarity between members of a pair. The three theoretical factors that may contribute to similarities and differences in behavior are genetic, common environmental, and separate environmental influences. Formally, the correlation between the phenotypic behaviors of the two members of the pair ($r_{P_1P_2}$) is stated as follows:

$$r_{P_1P_2} = h^2 r_{G_1G_2} + e_c^2 \qquad (9)$$

where h^2 is the "broad sense" heritability (Equation 2), $r_{G_1G_2}$ is the correlation between the genetic influences, and e_c^2 reflects the proportion of the variance in the behavior which is attributable to common environmental influences. The difference between the two members of a pair is expressed by:

$$1 - r_{P_1P_2} = h^2(1 - r_{G_1G_2}) + e_s^2 \qquad (10)$$

Here, e_s^2 is the coefficient reflecting that part of the variance which is due to non-shared environmental influences. From a practical measurement perspective, this term is inflated because it also includes the effect of any measurement error, which would reduce the estimate of the similarity in observed phenotype. When the relationships of Equations 9 and 10 are expressed in terms of variance and covariance rather than in the correlation metric, the formulae change somewhat. Since $h^2 = V_G/V_P$, $e_c^2 = V_{E_c}/V_P$, and $r_{P_1P_2} = \text{Cov } P_1P_2/V_p$, Equation 9 becomes:

$$\text{Cov } P_1P_2 = \text{Cov } G_1G_2 + V_{E_c} \qquad (11)$$

Where Cov P_1P_2 is the phenotypic covariance between individuals in the pair, Cov G_1G_2 is the covariance between genetic influences for one member of the pair and those for the other member of the pair, and V_{E_c} is the variance of the common environmental influences. Similarly, in covariance metric, Equation 10 becomes:

$$V_P - \text{Cov } P_1P_2 = V_G - \text{Cov } G_1G_2 + V_{E_s} \qquad (12)$$

where V_P − Cov P_1P_2 reflects the residual, or dissimilarity between phenotypes.

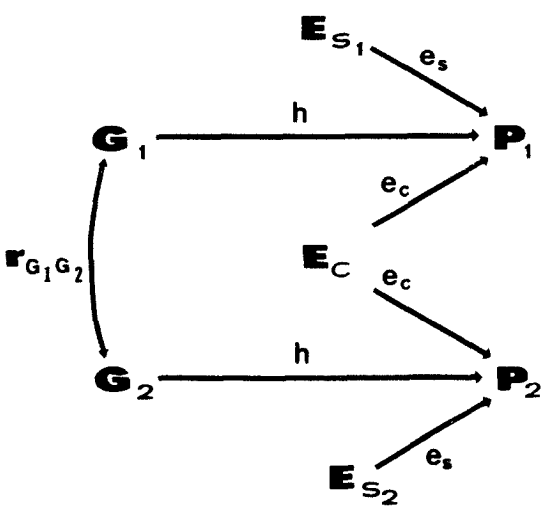

Figure 1. Path diagram depicting the theoretical contributions of heredity (G_1 and G_2) and of common environmental (E_c) and separate environmental (E_{s1} and E_{s2}) influences on phenotypic measures on a pair of individuals (P_1 and P_2). $r_{G_1G_2}$ reflects the extent to which the two individuals in a pair are genetically related.

Between and Within Components of Variance

In the study of sets of matched pairs, as in the present case, it is possible to decompose variance (such as phenotypic variance, V_P) into between and within components (Winer, 1971). Theoretically, the between-sets component of the variance is equal to the covariance of the phenotypic values of the pairs. Therefore, from Equation 10, we have:

$$\sigma_B = \text{Cov } G_1G_2 + V_{E_c} \qquad (13)$$

Similarly, the within-sets variance is equal to the difference between the total phenotypic variance and the covariance of the phenotypic values of the pairs. Equation 11, with this substitution, becomes:

$$\sigma_W^2 = V_G - \text{Cov } G_1G_2 + V_{E_s} \qquad (14)$$

Mean Squares Estimates

With a sample of twins, non-twin siblings, and unrelated individuals reared together, it is possible

to estimate the variance in phenotypic values between pairs of individuals and within pairs by using the traditional random effects ANOVA model (Kirk, 1982). The derived MS_W (mean squares within) from the analysis of variance is the best estimate of the within-pairs variance in behavior (σ_W). The MS_B (mean squares between) is estimated as twice the between-pairs variance plus the within-pairs variance ($2\sigma^2_B + \sigma^2_W$) (Glass & Stanley, 1970).

Expected Mean Squares

It is possible to postulate expected relative magnitudes of variance for the genetic and environmental influences that affect the phenotypic variance. Using the relationships between mean squares and variances discussed above, these are translated to expected mean squares between and within pairs (Fulker, Eysenck, & Zuckerman, 1980; Jinks & Fulker, 1970).

The expected mean squares coefficients for a study with the four groups of differently related subjects we have discussed are presented in Table 2 for each of the five influences. Columns marked G_A, E_c, and E_s reflect additive genetic effect, common environmental influence, and specific environmental influence, respectively. The columns G_D and E_T reflect the effects of dominance and of a special twin environmental influence. These are discussed more fully below.

The coefficients in Table 2 reflect the relative components of variance contributing to the observed between- and within-pairs variances (Mather & Jinks, 1977). The "2.0" under the additive genetic effect (G_A) for the MS_B expected for identical twins, along with the corresponding "0.0" for the expected MS_W, indicates that all of the variance due to additive genetic effects should be found in the variance between subject pairs. No variance within pairs can be due to genetic variation. The numbers "2.0" and "0.0" are derived in the following manner: The expected variance between pairs which is due to additive genetic effects should equal all of the variance caused by additive genetic effects. Similarly, the expected variance within pairs which is due to additive genetic effects should be zero; additive genetic variance does not contribute to differences between identical twins. The expected mean squares coefficient for the additive genetic component, then, is equal to 2.0, since the between component of variance is counted twice and the within component is zero.

The "1.5" for MS_B in the additive genetic effects column for the fraternal twins, coupled with the "0.5" associated with the MS_W, is derived in a similar manner. Because DZ twins share, on average, half of their genes, the proportion of variance between pairs due to additive genetic influences should be half that observed for MZ twins. Similarly, the additive genetic effect should manifest itself by causing an equal variation within pairs, since half of their genes are different. The MS_B coefficient in this case is $2(0.5) + 0.5 = 1.5$, while the MS_W coefficient is equal to 0.5. The remaining expected mean squares are derived in a similar manner from the expected variance due to the degree of genetic similarity of the pair or the similarity in the type of environment that is involved.

Table 2

Expected mean squares coefficients for each group of subjects

Groups	Type of Mean Square	Effect Coefficients				
		G_A	G_D	E_c	E_T	E_s
Identical Twins (MZ)	Between	2.0	2.0	2.0	2.0	1.0
	Within	0.0	0.0	0.0	0.0	1.0
Fraternal Twins (DZ)	Between	1.5	1.25	2.0	2.0	1.0
	Within	0.5	0.75	0.0	0.0	1.0
Non-twin Siblings	Between	1.5	1.25	2.0	1.0	1.0
	Within	0.5	0.75	0.0	1.0	1.0
Unrelated Adoptees	Between	1.0	1.0	2.0	1.0	1.0
	Within	1.0	1.0	0.0	1.0	1.0

Nonadditive Genetic Effects

We are also able to establish mean squares for nonadditive genetic effects. Genetic variation may be decomposed into three components: additive genetic effects (which we have described above), dominance effects, and polygenic epistatic effects. Since there are no differences in genes between identical twins, dominance and epistatic effects contribute completely to phenotypic similarity. On the other hand, because fraternal twins and non-twin siblings are not genetically identical, such nonadditive effects can make the pairs less similar phenotypically than they would be expected to be on the basis of their additive genotypic similarity. The extent of the effect is difficult to determine. If complete dominance is at work, the expected between-pairs variation for the DZ twins and non-twin siblings which is due to genetic similarity is about one-fourth that for the MZ twins, with three-fourths of the variation appearing within pairs. Similarly, it is difficult to determine the magnitude of epistatic effects; however, phenotypic similarity due to nonadditive genetic effects will quickly drop to near zero when more than a few genes are involved in the epistatic interaction. In the present example, our expected MS_B and MS_W coefficients (Table 2) for nonadditive effects are based on the assumption of a single-allele dominance effect or a two-allele epistatic effect.

Special Twin Environmental Effects

In comparison with non-twin siblings, twins might be treated more similarly, spend more time together, and be more often in similar situations (e.g., the same school class). It is therefore reasonable to expect that they share more common environmental influences than do non-twin siblings. It is also reasonable to expect that this special environmental similarity can give rise to more similar behavior than would be observed between non-twins. The extent of the special twin environment should be about the same for identical and fraternal twins, but should be absent completely for non-twin siblings and adoptees reared together. On the basis of these expectations, relative MS_B and MS_W can be derived as indicated in Table 2.

Solving the Simultaneous Equations

The problem we have defined involves the estimation of parameters in simultaneous equations. In our example we have four groups of differently related individuals, which provide eight points of information—observed MS_B and MS_W for each group. We have theoretically decomposed the mean squares into the various genetic and environmental contributions to the observed mean squares as would be expected for each group of subjects. The eight equations for these groups are presented in Table 3. Note that there are only five "unknowns" in the eight equations. Consequently, it is possible to derive a maximum likelihood solution to the parameters. A number of minimization routines are available which can provide estimates. One of these is a simplified LISREL (Jöreskog & Sörbom, 1978) model (Fulker, Baker, & Bock, 1983; McArdle, Goldsmith, & Horn, 1982).

Once the equations are solved, the sum of variances (additive, dominance, common, special twin, and separate environmental) will reflect the total variance. The ratio of the sum of the genetic terms (additive genetic variance and dominance genetic variance) to the total variance should reflect the broad sense heritability (Falconer, 1981) of the characteristic. The ratio of the environmental terms to the total variance should reflect the environmentality (Fuller & Thompson, 1978). Note that the inclusion of the dominance genetic effect and the special twin environmental effect will permit heritability and environmentality to reflect more correctly the hereditary and environmental influences than the classical approaches would have permitted.

Table 3

Simultaneous equations

MS_{BMZ}	= 2.00 V_A	+ 2.00 V_D	+ 2.00 V_c	+ 2.00 V_T	+ 1.00 V_s
MS_{WMZ}	=				1.00 V_s
MS_{BDZ}	= 1.50 V_A	+ 1.25 V_D	+ 2.00 V_c	+ 2.00 V_T	+ 1.00 V_s
MS_{WDZ}	= 0.50 V_A	+ 0.75 V_D	+		1.00 V_s
MS_{BSibs}	= 1.50 V_A	+ 1.25 V_D	+ 2.00 V_c	+ 1.00 V_T	+ 1.00 V_s
MS_{WSibs}	= 0.50 V_A	+ 0.75 V_D	+	1.00 V_T	+ 1.00 V_s
MS_{BADP}	= 1.00 V_A	+ 1.00 V_D	+ 2.00 V_c	+ 1.00 V_T	+ 1.00 V_s
MS_{WADP}	= 1.00 V_A	+ 1.00 V_D		1.00 V_T	+ 1.00 V_s

An Example

Returning to our earlier examples with Professor Plomin's HR data, we will attempt to illustrate the procedure we have just described. These data included only MZ and DZ twins, but we will add fictional groups of non-twin siblings and pairs of adoptees who have been raised together. We do this in order to illustrate the informational advantage of using additional differently related groups. Of course, the procedure could just as easily be completed with just the two groups of twins, but under these conditions we could not estimate the importance of nonadditive genetic effects or special twin environmental effects.

With the four groups of subjects—MZ twins, DZ twins, non-twin siblings, and adoptees reared together—the expected mean squares coefficients are as expressed in Table 2, and the simultaneous equations to be solved are those presented in Table 3. The observed mean squares (MS), of course, are estimated empirically. Usually, as indicated above, these are estimated with the traditional random effects ANOVA model. We often use the SPSS (Nie, Hull, Jenkins, Steinbrenner, & Bent, 1975) ONEWAY procedure for this, but many alternatives are available. Having the mean squares we proceed to obtain maximum likelihood estimates of the unknown parameters in the simultaneous equations of Table 3, the parameters reflecting the component of variance associated with each of the genetic and environmental influences. Several minimization programs are available for this estimation. We use the LISREL program noted above by using a Y-only model, and fixing the error terms to zero. By using a multiple group setup, we are able to simultaneously solve a series of expressions of the following model:

$$MS_O = \Lambda \Psi \Lambda' \qquad (15)$$

Where Ψ is a diagonal matrix of the expected mean square coefficients (Table 2) and Λ is a row vector of the estimable genetic and environmental effect terms. MS_O, of course, is the column vector of observed mean squares (Table 3). Hypothetical model estimates for the genetic and environmental components are given in Table 4 for three hypothetical variables, HR level, HR response, and shyness.

Table 4

Hypothetical model estimates of the genetic and environmental components of the variation of three variables and the proportion of variance associated with each variable

Variables	Biometrical Model Estimates				
	G_A	G_D	E_c	E_T	E_s
HR Level	.5 (.58)[a]	.2 (.09)	.2 (.09)	.1 (.02)	.3 (.21)
HR Response	.7 (.73)	.3 (.13)	.2 (.06)	.1 (.01)	.2 (.06)
Shyness	.2 (.09)	.1 (.02)	.4 (.34)	.5 (.53)	.1 (.02)

[a]Numbers in parentheses reflect the proportion of variance associated with each component.

Table 5

Mean squares, parameter estimates, and estimates of proportion of variance explained by each component

Mean Squares for the Variable Heart Rate Level					
Type	MZ Males	MZ Females	DZ Males	DZ Females	DZ Opposite Sex
Between	228.967	146.179	203.260	97.215	84.355
Within	39.232	66.995	70.300	72.616	42.706

Parameter Estimates			
σ_A	σ_{E_s}	$\sigma_{E_{c(males)}}$	$\sigma_{E_{c(females)}}$
6.30	7.22	5.79	.00

Proportion of Variance Explained by Each Component			
G_A	E_s	$E_{c(males)}$	$E_{c(females)}$
.23	.45	.27	.00

These estimates are the values of Λ as derived in the model. Their squares must, therefore, reflect the variances associated with each of the components. We can now estimate heritabilities for each of our variables. These are presented in Table 4 also.

Additional Points

In our examples we have either assumed that there is no sex difference, or we have corrected for observed sex differences. However, there are times when a psychophysiologist might wish to take sex differences into account. These differences may be caused by a difference in genetic influences for males and females, or by a difference in environmental influences. In the study of twins, MZ pairs will always be of the same sex, and so one will have two groups of MZ twins, female and male MZ twin pairs. With DZ twin groups an additional group must be considered, the mixed sex group. The inclusion of a sex difference is easy to accomplish with the biometrical model. One would derive MS estimates within each of the five subgroups rather than for only two groups. Assuming a sex difference in genetic influences we estimate separate V_A's for males and females. Likewise, if we assume a difference in common environmental influences we estimate separate V_{Ec}'s for males and females.

Returning again to Professor Plomin's data we can illustrate this point. Using only the actual acquired data on HR level from the MZ and DZ twins, but analyzing separately by sex, we obtained the mean squares presented in Table 5. Evaluating the data as described above, we found that a model with separate common environmental influences for males and females gave the best fit. Parameter estimates for this model are presented in Table 5, along with the proportions of variance contributed by each of the influences. As the results suggest, there is more variability in HR level among males than among females. The separate environmental and genetic influences appear to make important contributions, while common environmental factors appear to be significant for males only.

An example of a multivariate extension of a model involving sex differences can be found in Martin, Eaves, and Fulker (1979).

The Multivariate Biometrical Approach

As we noted above, the psychophysiologist might wish to know the genetic and environmental contributions to the covariance between two or more variables. The biometrical approach to analyses of psychophysiological data can be extended to the multivariate case as the classical approach was extended to the multivariate case. A good introduction to multivariate extensions of biometrical approaches is provided by Fulker (1978).

In the case of twin data (although the procedure generalizes to comparisons of any genetically related groups), between- and within-pair mean squares and cross-products can be derived when several measures are involved by using MANOVA. MANOVA will give four matrices: the MZ and DZ between and the MZ and DZ within variance/covariance matrices. These four matrices can be equated to their expected matrices as in the univariate case discussed above. We then get:

$$2A + 2C + S \text{ for the between MZ matrix,} \quad (16)$$

$$S \text{ for the within MZ matrix,} \quad (17)$$

$$1.5A + 2C + S \text{ for the between DZ matrix,} \quad (18)$$

and

$$0.5A + S \text{ for the within DZ matrix.} \quad (19)$$

A, C, and S are the genetic, common environmen-

tal, and specific environmental variance/covariance matrices, respectively. As we have done in the univariate case, we equate our observed matrices to the expected matrices. By solving for the four matrix equations simultaneously, we obtain estimates for **A**, **C**, and **S**. These variance/covariance matrices then can be rescaled as correlation matrices.

Let us return once more to our example of HR response measured under two different task conditions (HRR1 and HRR2). In this example we include only MZ and DZ twin pairs, but the multivariate solution we employ would permit us to include other groups as we did in the univariate example.

To begin our analyses we generate estimates of the Mean Squares and Cross-Products (MSCP) matrices between and within pairs of subjects for each of the differently related groups of subjects. Usually we obtain Sum of Squares and Cross-Products (SSCP) matrices by using the SPSS procedure MANOVA (Hull & Nie, 1981) and then divide the matrices by the degrees of freedom for each group to obtain the MSCP matrices. We then obtain maximum likelihood estimates of the parameter matrices of equations 16 through 19. One way to estimate the matrices is the method of Fulker et al. (1983) using LISREL. The resulting matrices **A**, **C**, and **S** are covariance matrices of the additive genetic, common environmental, and separate environmental components of the variables, respectively. The diagonals of the covariance matrices are the components of variation associated with each variable. The covariance matrices are usually rescaled to correlation matrices. Table 6 presents the correlation matrices for our two variables, HRR1 and HRR2. As can be seen, the maximum likelihood estimates are quite close to the estimates obtained by the cross-correlational method.

Discussion

Evidence from psychophysiological studies has demonstrated that genetic factors play some role in resting levels and responses to stimuli. Because of these findings, it is reasonable for psychophysiologists to consider the genetic and environmental contributions to observed variations in physiological measures.

We have outlined univariate and multivariate classical and biometrical approaches as these might be employed to estimate these contributions. All that is required is that the psychophysiologist include groups at different levels of genetic relatedness as part of the subject group. In doing this, nothing will be lost over analysis of all unrelated subjects, while the additional information about individual differences will be gained.

More complicated models and analyses than those described in this paper are necessary when gene-environment interactions (Plomin, DeFries, & Loehlin, 1977) or very complicated genetic influences are involved, but the analyses we have presented will be adequate for most purposes.

The use of such techniques, which have demonstrated genetic contributions to certain cardiovascular variables and EEG characteristics, has been important in the study of psychophysiological risk factors. For instance, the finding of a relationship between genetically influenced cardiovascular variables and risk for cardiovascular disease (Feinleib et al., 1977; Havlik & Feinleib, 1982) has demonstrated a potential genetic etiology for the disease, as well as suggested the possible mechanism by which the genetic influence is related to the outcome. In studies of genetic risk for alcoholism, heritable EEG characteristics have been found to be characteristic of individuals at high risk for the development of alcoholism, before and in response to alcohol (Gabrielli et al., 1982; Pollock et al., 1983; Propping, Kruger, & Mark, 1981). These findings are important because they indicate how individuals at high risk for alcoholism may differ in brain characteristics from individuals who are at low risk and consequently may explain why they are at higher genetic risk for the disorder. Progress can be made in studies such as these by knowing the extent to which a characteristic is heritable and the extent to which the heritable component is related to that of another characteristic.

It is clear from our examples that an understanding of the genetic and environmental factors that contribute to the etiology of psychophysiological characteristics can make an important contribution to our knowledge about the involvement of these factors in the development of psychopathologies or other diseases. It is also obvious that this principle generalizes to the understanding of how psychophysiological measures are related to behavior in general.

Table 6

Maximum likelihood estimates of component correlation matrices for HRR1 and HRR2

	Maximum Likelihood Estimates		
Variables	Additive Genetic Component	Common Environmental Component	Separate Environmental Component
HRR1	1.0	1.0	1.0
HRR2	.96 1.0	.95 1.0	.68 1.0

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