Scope and Methodology of Twin Studies

SCOPE AND METHODOLOGY OF TWIN STUDIES

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Twin research has not become obsolete as its critics of twenty years ago perhaps expected it would. Old, familiar research designs are finding new applications, and new research designs are appearing. Of greatest interest are the epidemiological studies that depend on the assembly or the aging of large numbers of twins in twin registries. As an outgrowth partly of the twin registries, partly of conceptual and mathematical progress, new methods have emerged for diagnosis of twin types and for analysis of twin data. One line of development started with the questionnaire method of zygosity diagnosis and has given rise most recently to zygosity diagnosis by principal component analysis. Another line started with probability calculations and has led to the use of generalized distance and noncentral chi-square. The appropriateness of these methods in different contexts needs to be critically reviewed.

Among numerous research attacks on the phenomenon of twinning, some have potential impact on the " experimental " uses of twins. A good example is the analysis of the peculiarities of the environment of twins, which is of course very important in psychological twin research.

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APPLICATIONS AND PERSPECTIVES OF TWIN STUDIES IN POPULATION GENETICS

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The study of populations and of twin samples as a method of human genetic research today still has, for the majority of human geneticists, the same meaning that it had in 1876 when Galton published his *History of Twins as a Criterium of the Relative Powers of Nature and Nurture.*

For a more complete evaluation of the possibility of research originating from an experimental twin plane, a quick survey is made of the present development of the methods connected with the problem of the relationship between heredity and environment, to then pass to examine the probability offered by twin data to solve problems of population genetics, such as the appraisal of genotypic and genic frequencies, the establishment of transmission models, the calculation of penetrance, linkage estimate, and mutation rate.

Finally, and as a suggestive perspective, it is stressed how twins may be used for the analysis of genetic distance.

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DOWN'S SYNDROME IN TWINS: LACK OF EVIDENCE FOR INDEPENDENCE OF NONDISJUNCTION AND DIZYGOTIC TWINNING

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An hypothesis is examined which considers the assumption of twin methodology that only two modes of twinning exist. The null hypothesis that DZ twinning and concordance for Down's syndrome are independent events is tested after removal of effects such as covariance due to maternal age. The null hypothesis is rejected ($P < 0.000002$).

Possible explanations of the result considered are (*a*) that some of the cases are MZ

twins, (b) that some of the cases are of the translocation mode, (c) that another mode of twinning exists (uniovular dispermatic twins), and (d) that an assumption of the test is violated. It is shown that explanation (c) is an equally likely predictor of the test result.

If uniovular dispermatic twins exist, it is estimated that they would constitute only about 1% of a random sample of twins, and their incidence in the general population is estimated to be about 9.6×10^{-5}. It is suggested that this alleged form of twinning be considered as a mutational event, rather than as a " mode " of twinning.

These estimations suggest that twin methodology would not be appreciably biased if alleged uniovular dispermatic twins were included in the test sample.

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THE PROBLEM OF GENOTYPE × ENVIRONMENT COVARIANCE IN THE ESTIMATION OF HERITABILITY FROM MZ AND DZ TWINS

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It is commonly, but incorrectly, assumed that the presence of genotype × environment covariance must necessarily reduce the heritability (h^2) as estimated from twin data, when the formula used to obtain h^2 makes no assumption about G × E covariance or assumes that it is zero. But, in fact, G × E covariance does not always reduce the genetic variance, and it can be shown under some conditions, an increase in the G × E covariance implies a greater genetic variance. The effect of G × E covariance on h^2, as estimated from data on MZ and DZ twins, depends jointly upon the degree of assortative mating and the degree of environmental correlation between MZ twins and between DZ twins. A method, based on the solution of a pair of simultaneous quadratic equations, is proposed for estima-

ting the range of h^2 from twin data under varying assumed values for assortative mating, the environmental correlations between MZ and DZ twins, and the G × E covariance. The solution of three simultaneous equations permits direct estimation of the genetic variance, environmental variance, and G × E covariance, under varying reasonable assumed values for assortative mating and the MZ and DZ environmental correlations. Examples of the method are based on intelligence test scores of MZ and DZ twins.

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ANALYSIS OF TWIN DATA AND ESTIMATION OF HERITABILITY EFFECTS

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In a statistical sense, the objective of twin research is to partition the variance on some criterion measure among genetic and environmental factors. Although certain elaborate models have been developed, these models do not supply a convenient test statistic to show which factors make a significant contribution. Consequently several procedures drawn from analysis of variance have been adapted for use with twin data. The general case is illustrated below.
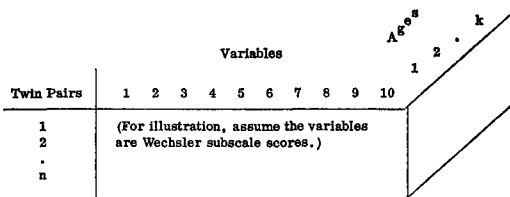
This design provides for the analysis of data that has been collected at successive ages, as in longitudinal studies; and it also pro-