GENETIC DISSECTION OF A COMPLEX TRAIT: BINARY END-POINTS VERSUS MULTIVARIATE PHENOTYPES

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A complex trait is usually a function of a multivariate phenotype comprising correlated quantitative variables. Since end-point traits are usually binary in nature (affected/unaffected) and hence contain minimal information on variation within trait genotypes, it may be statistically more powerful to use a correlated multivariate phenotype for identifying genes for the complex trait. Mapping a multivariate phenotype traditionally uses some function of quantitative values of sib-pairs or other sets of relatives as a response variable and marker IBD scores as explanatory variables and is thus susceptible to violations in distributional assumptions. We propose, along the lines of Sham et al. (2002), a linear regression formulation in which the response and explanatory variables are interchanged. Analyses do not require modeling the covariance structure of the multivariate phenotype vector or any data reduction technique such as principal components. It can simultaneously incorporate qualitative and quantitative traits and can use data on n siblings as (n-1) independent observations. Using simulations under different models, we find that the proposed method is more powerful than the Haseman-Elston regression and the reverse regression procedures based on (i) the first principal component of the correlated phenotypes and (ii) the end-point binary trait. An application of the method is illustrated using data on alcoholism related phenotypes from the COGA study.