Robust Variance-Components Approach for Assessing Genetic Linkage in Pedigrees

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SUMMARY

To assess evidence for genetic linkage from pedigrees, I developed a limited variance-components approach. In this method, variability among trait observations from individuals within pedigrees is expressed in terms of fixed effects from covariates and effects due to an unobservable trait-affecting major locus, random polygenic effects, and residual nongenetic variance. The effect attributable to a locus linked to a marker is a function of the additive and dominance components of variance of the locus, the recombination fraction and the proportion of genes identical by descent at the marker locus for each pair of sibs. For unlinked loci, the polygenic variance component depends only on the relationship between the relative pair. Parameters can be estimates by either maximum-likelihood methods or quasilikelihood methods. The forms of quasilikelihood estimators are provided. Hypothesis tests derived from the maximum-likelihood approach are constructed by appeal to asymptotic theory. A simulation study showed that the size of likelihood-ratio tests was appropriate but that the monogenic component of variance was generally underestimated by the likelihood approach.

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