Hsiung, Chao A. (National Health Research Institutes, Taiwan, R.O.C.)

Incorporating Endophenotypes into Allele-Sharing Based Linkage Tests

Abstract: For a genetic study in which there are concordant and discordant sibpairs for a complex disease trait and there are also available the measurements of other endophenotypes/intermediate phenotypes for each of the individuals, we describe an allele-sharing based multipoint linkage test that utilizes nonparametrically the additional endophenotypes/intermediate phenotypes. The usefulness of this method is evaluated in simulation studies, which show that the gain in power is influenced by not only the endophenotypic value but also the correlation between the diagnosis-based phenotype and the endophenotype. In addition to reporting p-values, our method also provides an index C_E, derived from the coefficients of the weight function associated with the endophenotype in the proposed statistic, to indicate the relevance of a specific endophenotype/intermediate phenotype in the genetic study. The simulation study indicates that larger power, in general, corresponds to larger value of the index C_E. The index C_E is thus suggested as a quantity to be used in the choice of endophenotypes in linkage study. Data from the Stanford Asian Pacific Program in Hypertension and Insulin Resistance (SAPPHIRe) are used to illustrate the method.