ROBUST TDT-TYPE ASSOCIATION TESTS AGAINST GENOTYPING ERROR

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The transmission/disequilibrium test (TDT), a family based test of linkage and association , is a popular test for studies of complex inheritance, as it is nonparametric and robust against spurious conclusions induced by hidden genetic structure, such as stratification or admixture. However, the TDT may be biased by genotyping error. Undetected genotyping errors may be contributing to an inflated type I error rate among reported TDT-derived associations. In this paper, we consider an allele-based random error model for describing the pattern of genotyping errors and show how to construct two robust TDT-type association tests against genotyping error. The first test is an adjusted TDT which is appropriate when Hardy-Weinberg equilibrium holds. The second test is a nonparametric test and also robust against population stratification. Moreover, this test does not need to assume allelic error rates to be constant across families in the analysis. The two test statistics are very easy to compute. Simulation studies confirm that the two tests have very reasonable performance.