ABSTRACT

Several investigators have proposed tests for genetic association based on data from nuclear families. The tests differ in how they handle missing parental genotypes. I shall discuss three of these tests (the FBAT test proposed by Rabinowitz and Laird (2000), a second test proposed by Rabinowitz (2002), and the FGAP Nonfounder or partial score test proposed by Clayton (1999) and Whittemore and Tu (2000)). Each test statistic arises from the efficient score of the family data as the solution to a set of constraints on its null expectation. Moreover the FBAT and Rabinowitz tests (but not the FGAP test) are locally most powerful among all tests satisfying their constraints. I shall show the results of simulations to evaluate the size and power of the tests in various settings. In the simulations, the FBAT test tended to have less power than the other two tests, particularly when applied to families in whom all offspring were affected. Both the Rabinowitz test and the FGAP Nonfounder test performed comparably, although the FGAP test tended to extract more information from families containing one typed parent. While none of the tests showed good power to detect rare recessively acting genes, the Rabinowitz test performed particularly poorly in this case. Nevertheless for large numbers of families, the Rabinowitz test has good power to detect dominant or additive alternatives without forfeiting robustness against misspecification of parental genotype probabilities.