Sib transmission and disequilibrium tests for linkage and/or association using multiple highly linked markers

Jinheum Kim[1]

[1] Department of Applied Statistics, University of Suwon, Korea

Family-based tests such as the transmission and disequilibrium tests(TDT) have proved to be powerful tools in the search for disease genes. Unlike case-control studies, the tests are not affected by population admixture, which can lead to spurious association of multiple highly linked makers with disease-susceptible genes. Those tests have largely required knowledge of parental marker genotypes. However, parental data are often not available for late-onset diseases. In this article we propose sib-TDTs that overcome this problem by use of marker data from unaffected sib(s) instead of parents. To do this end, we first defined a Mantel-Haenszel-type statistic for each haplotype and then proposed two tests based on this statistic. If the haplotype pair of each subject were to be uniquely resolved, a transmission and non-transmission table would be deterministic and thereby the proposed test could be reduced to the test proposed by Schaid and Rowland[2]. Otherwise, we need to reconstruct the transmission and non-transmission table using the method proposed by Zhao et al.[3] and Kim et al.[1]. Simulation studies suggest that the proposed tests are robust to population admixture and are monotone increasing as a relative risk increases irrespective of mode of inheritance. We also illustrated the proposed tests with data adopted from Yonsei Cardiovascular Genome Center

References

[1] Nam CM, Kang DR, Kim J (2006) Haplotype-based score test for linkage in nuclear families. BMC Bioinformatics 8(277):1-7.

[2] Schaid DJ, Rowland C (1998) Use of parents, sibs and unrelated controls for dection of associations between genetic markers and disease. American Journal of Human Genetics 63:1492-1506.

[3] Zhao H, Zhang S, Merkikangas KR, Trixler M, Wildenauer DB, Sun F, Kidd KK (2000) Transmission/disequilibrium tests using multiple tightly linked markers. American Journal of Human Genetics 67:936-946.