Abstract

Genome-wide Association Studies (GWASs) for complex diseases often collect data on multiple correlated endo-phenotypes. Multivariate analysis of these correlated phenotypes can improve the power to detect genetic variants. Multivariate analysis of variance (MANOVA) can perform such association analysis at a GWAS level, but the behavior of MANOVA under different trait models have not been carefully investigated. In this paper, we show that MANOVA is generally very powerful for detecting association but there are situations, such as when a genetic variant is associated with all the traits, where MANOVA may not have any detection power. We investigate the behavior of MANOVA, both theoretically and using simulations, and derive the conditions where MANOVA loses power. Based on our findings, we propose a unified score-based test statistic USAT that can perform better than MANOVA in such situations and do almost as good as MANOVA elsewhere. Our proposed test reports an approximate asymptotic p-value for association and is computationally very efficient to implement at a GWAS level. We have studied through extensive simulation the performance of USAT, MANOVA and other existing approaches and demonstrated the advantage of using the USAT approach to detect association between a genetic variant and multivariate phenotypes.