Growth Mixture Modeling as an Exploratory Analysis Tool in Longitudinal QTL Analysis

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Abstract

We examined the properties of growth mixture modeling (GMM) in finding longitudinal quantitative trait loci in a genome wide association study. Two software packages are commonly used in these analyses: Mplus and the SAS TRAJ procedure. We analyzed the 200 replicates of the simulated data derived from the Framingham Heart Study data set for 6,476 subjects with these programs using three tests: the likelihood ratio test statistic (LRTS), a direct test of genetic model coefficients, and the chi-square test classifying subjects based on the trajectory model's posterior Bayesian probability. The Mplus program was not effective in this application due to its computational demands. The distributions of these tests applied to genes not related to the trait were sensitive to departures from Hardy-Weinberg equilibrium. The LRTS was not usable in this application in that its distribution was far from the expected asymptotic distributions when applied to markers with no genetic relation to the quantitative trait. The other two tests were satisfactory. Power was still substantial when markers near the gene rather than the gene itself were used. That is, GMM may be useful in genome wide association studies. For markers near the actual gene, there was somewhat greater power for the direct test of the coefficients and lesser power for the posterior Bayesian probability chi-square test.