

A Fast and powerful eQTL weighted method to detect genes associated with complex trait using GWAS summary data

Xuexia Wang

UNIVERSITY OF NORTH TEXAS

E-mail: Xuexia.Wang@unt.edu

Abstract: Although genome-wide association studies (GWASs) have identified many genetic variants underlying complex traits, a large fraction of heritability still remains unexplained. Integrative analysis that incorporates additional information such as expression quantitative trait locus (eQTL) data into sequencing studies (denoted as transcriptome-wide association study TWAS) can aid the discovery of trait associated genetic variants. However, general TWAS methods only incorporate one eQTL-derived weight (e.g. cis-effect), and thus can suffer substantial loss of power when the single estimated cis-effect is not predictive for the effect size of a genetic variant or there are estimation errors in the estimated cis-effect, or even if the data is not consistent with the model assumption. In this study, we propose an omnibus test which utilizes a Cauchy association test to integrate association evidence demonstrated by three different traditional tests (Burden test, Quadratic test and Adaptive test) using GWAS summary data with multiple eQTL-derived weights. The p value of the proposed test can be calculated analytically, and thus it is fast and efficient. We applied our proposed test to two schizophrenia (SCZ) GWAS summary datasets and two lipids trait (HDL) GWAS summary datasets. Compared to the three traditional tests, our proposed omnibus test can identify more trait-associated genes.