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Multitrait transcriptome-wide association study (TWAS) tests

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Abstract

Multitrait tests can improve power to detect associations between individual single-nucleotide polymorphisms (SNPs) and several related traits. Here, we develop methods for multi-SNP transcriptome-wide association (TWAS) tests to test the association between predicted gene expression levels and multiple phenotypes. We show that the correlation in TWAS test statistics for multiple phenotypes has the same form as multitrait statistics for the single-SNP setting. Thus, established methods for combining single-SNP test statistics across multiple traits can be extended directly to the TWAS setting. We performed an extensive evaluation across eight multitrait methods in simulations that varied gene-phenotype effect sizes in addition to the underlying covariance structure among the phenotypes. We found that all multitrait TWAS tests have well-