

Genome-wide Association Testing for Pleiotropic Effects using GWAS Summary Statistics

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Abstract: It has been empirically observed that many human complex traits are genetically correlated, indicating that a single gene might affect multiple phenotypes. This biological phenomenon is referred to as “pleiotropy”, which is of increasing scientific and medical interests for precision medicine and drug repurposing. However, there are very few statistical methods available for detecting such pleiotropic genetic variants. We note that the null hypothesis of no pleiotropic effect is composite and thus imposes great statistical challenges. In this paper, we develop a novel pleiotropic effect test (PET) to detect SNPs with pleiotropic effects on two phenotypes by taking the composite null issue into account. Extensive simulation studies show that our method maintains correct type I error rate and is well powered. We also apply the PET to the global lipids GWAS data sets and detect many novel pleiotropic SNPs affecting lipids traits. We also develop an user-friendly and computationally efficient R package PET for public use.