

Abstract: A multi-stage variable selection method is introduced for detecting association signals in structured brain-wide and genome-wide association studies (brain-GWAS). Compared to conventional single-voxel-to-single-SNP methods, our approach is more efficient and powerful in selecting the important signals by integrating anatomic and gene grouping structures in the brain and the genome, respectively. It avoids resorting to large number of multiple comparisons while effectively controlling the false discoveries. Validity of the proposed approach is demonstrated by both theoretical investigation and numerical simulations. We apply our proposed method to a brain-GWAS using ADNI PET imaging and genomic data. We confirm previously reported association signals and also uncover several novel SNPs and genes that either are associated with brain glucose metabolism or have their association significantly modified by Alzheimer's disease status.