

Multi-trait genome-wide association analysis of blood pressure identifies 45 additional loci

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Introduction:

Single-trait genome wide association studies (GWAS) have revealed over 1,000 blood pressure (BP) loci. However, these loci only account for less than one third of the BP genetic variation. Multi-trait GWAS is reported to increase discovery power by jointly analysing highly correlated traits. By performing the first large-scale multi-trait BP GWAS, we aimed 1) to compare multi-trait vs single-trait results and 2) identify additional loci.

Methods:

We apply MTAG to conduct a multi-trait GWAS of systolic BP, diastolic BP and pulse pressure using results from our recent GWAS discovery analysis of ~750k individuals of European ancestry from UK Biobank and the International Consortium of Blood Pressure. To detect additional loci we tested ~7 million imputed genetic variants applying the same combined 1-stage and 2-stage design criteria as in the original GWAS, with replication using MTAG results from the US Million Veteran Program (n~220k).

Results:

Single-trait GWAS yielded a higher number of significant independent signals genome-wide. Nevertheless, our multi-trait analysis identified 45 new BP loci that were not detected in the equivalent GWAS, of which nine remain novel (based on further BP loci discoveries since 2018).

Conclusions:

Our multi-trait GWAS discovered additional BP loci. However, our results illustrate that the benefits of MTAG are trait-specific, requiring high pairwise correlation between all pairs of traits, and that more power is gained when MTAG is also used for meta-analysis of traits from different samples. This suggests that future BP genetics discovery projects should focus efforts on larger meta-analyses including new cohorts.