

ADHD+DBDs GWAS meta-analysis results (Europeans only), January 2021 Release (iPSYCH+PGC data)

The file “ADHD_DBDs_GWAS_meta_January2021.gz” contains results from the GWAS meta-analysis of disruptive behavior disorders (DBDs) in the context of attention deficit hyperactivity disorder (ADHD).

Citation for studies using these data:

Ditte Demontis, Raymond K. Walters, Veera M. Rajagopal, Irwin D. Waldman, Jakob Grove, Thomas D. Als, Søren Dalsgaard, Marta Ribasas, Jonas Bybjerg-Grauholm, Maria Bækvad-Hansen, Thomas Werge, Merete Nordentoft, Ole Mors, Preben Bo Mortensen, ADHD Working Group of the Psychiatric Genomics Consortium (PGC), Bru Cormand, David M. Hougaard, Benjamin M. Neale, Barbara Franke, Stephen V. Faraone, Anders D. Børglum. ***Risk variants and polygenic architecture of disruptive behavior disorders in the context of attention-deficit/hyperactivity disorder.*** Nature Communications, 2021, <https://doi.org/10.1038/s41467-020-20443-2>

Disclaimer

These data are provided "as is", and without warranty, for scientific and educational use only. If you download these data, you acknowledge that these data will be used only for non-commercial research purposes; that the investigator is in compliance with all applicable state, local, and federal laws or regulations and institutional policies regarding human subjects and genetics research; that secondary distribution of the data without registration by secondary parties is prohibited; and that the investigator will cite the publication in any communications or publications arising directly or indirectly from these data.

Methods

See the article for full details. Briefly:

Genotyping, quality control and GWAS meta-analysis

The file contains results from the meta-analysis of the iPSYCH cohort and six ADHD cohorts (cohorts of European ancestry) provided by PGC with information about diagnoses of ADHD+DBDs. An overview of the cohorts including genotyping information and diagnosis criteria can be found in Supplementary Table 9, Demontis et al. Nature Communications, 2021 (<https://doi.org/10.1038/s41467-020-20443-2>).

Quality control, imputation and primary GWASs of the iPSYCH and PGC cohorts were done separately for each using the bioinformatics pipeline Ricopili. Pre-imputation quality control allowed an inclusion of individuals with a call rate > 0.98 (>0.95 for iPSYCH) and genotypes with a call rate >0.98, difference in SNP missingness between cases and controls < 0.02, no strong deviation from Hardy-Weinberg equilibrium ($P > 1 \times 10^{-6}$ in controls or $P > 1 \times 10^{-10}$ in cases) and low individual heterozygosity rates ($|F_{het}| < 0.2$). Genotypes were phased and imputed using SHAPEIT and IMPUTE2 and the 1000 Genomes Project phase 3 (1KGP3) as imputation reference panel. Trio imputation was done with a case-pseudocontrol setup.

Relatedness and population stratification were evaluated using a set of high-quality genotyped markers (minor allele frequency (MAF) >0.05, HWE $P > 1 \times 10^{-4}$ and SNP call rate >0.98) pruned for linkage disequilibrium (variants located in long-range LD regions defined by Price et al. were excluded). Genetic relatedness was estimated using PLINK v1.9 to identify first and second-degree relatives ($\hat{\pi} > 0.2$) and one individual was excluded from each related pair (cases preferentially retained over controls). Genetic outliers were excluded based on principal component analyses (PCA) using EIGENSOFT. For iPSYCH a genetic homogenous sample was defined based on a subsample of individuals being Danes for three generations. For the PGC samples genetic outliers were removed based on visual inspection of the first six PCs. For all cohorts PCA was redone after exclusion of genetic outliers.

Association analysis was done in PLINK using additive logistic regression and the imputed marker dosages, covariates from principal component analyses after removal of genetic outliers and other relevant covariates. Meta-analysis of the iPSYCH cohort (2,155 cases, 22,664 controls) and the six PGC cohorts (1,647 cases, 8,641 controls) was done using an inverse standard error weighted fixed effects model and the software METAL and included in total 3,802 cases and 31,305 controls.

File Description

ADHD_DBDs_GWAS_meta_January2021.gz: GWAS meta-analysis of ADHD+DBDs (2,387 CUD cases and 48,985 controls)

MD5 checksum (ADHD+DBDs_GWAS_meta_January2021.gz) =
b3b2e4feb112042ad792107315e6d10

CHR Chromosome (hg19)

SNP Marker name

BP Base pair location (hg19)

A1 Reference allele for OR (may or may not be minor allele)

A2 Alternative allele

INFO Imputation information score

OR Odds ratio for the effect of the A1 allele

SE Standard error of the log(OR)

P P-value for association test in the meta-analysis

Additional Notes

For long insertion/deletion variants, the A1/A2 alleles are truncated to the first 13 bases with a specification of the remaining length (e.g. AACACACACACAC+16)

The reported imputation INFO score is a weighted average across the cohorts contributing to meta-analysis for that variant

Allele frequencies and case/control counts per variant are currently omitted from public release for data privacy. For inquiries about accessing this data, please contact Ditte Demontis (ditte@biomed.au.dk).

Data Use Agreement

If you download these data, you and your immediate collaborators (“investigators”) acknowledge and agree to all of the following conditions:

1. These data are provided on an "AS-IS" basis, without warranty of any type, expressed or implied, including but not limited to any warranty as to their performance, merchantability, or fitness for any particular purpose;
2. Investigators will use these results for scientific research and educational use only;
3. The downloaded results can be shared among collaborators but the reposting or public distribution of the result file is prohibited;
4. Investigators certify that they are in compliance with all applicable local, state, and federal laws or regulations and institutional policies regarding human subjects and genetics research;
5. Investigators will cite the appropriate publication in any communications or publications arising directly or indirectly from these data; and
6. Investigators will never attempt to identify any participant.

Experience has taught us that the appropriate use of these data requires considerable attention to detail, prior experience, and technical skill. Errors are easy to make. If investigators use these data, any and all consequences are entirely their responsibility.