Differentiating ADHD vs ASD GWAS meta-analysis results (Europeans only), April 2022 Release (iPSYCH+PGC data)

The file "asdVSadhdWOid50_filtered_clean.gz" contains results from the differentiating GWAS meta-analysis of attention deficit hyperactivity disorder (ADHD, coded = 1) versus autism spectrum disorder (ASD; coded = 2).

Citation for studies using these data:

Manuel Mattheisen, Jakob Grove, Thomas D Als, Joanna Martin, Georgios Voloudakis, Sandra Meier, Ditte Demontis, Jaroslav Bendl, Raymond Walters, Caitlin E Carey, Anders Rosengren, Nora I Strom, Mads Engel Hauberg, Biao Zeng, Gabriel Hoffman, Wen Zhang, Jonas Bybjerg-Grauholm, Marie Bækvad-Hansen, Esben Agerbo, Bru Cormand, Merete Nordentoft, Thomas Werge, Ole Mors, David M Hougaard, Joseph D Buxbaum, Stephen V Faraone, Barbara Franke, Søren Dalsgaard, Preben B Mortensen, Elise B Robinson, Panos Roussos, Benjamin M Neale, Mark J Daly, Anders D Børglum ***Identification of shared and differentiating genetic risk for autism spectrum disorder, attention deficit hyperactivity disorder and case subgroups.*** https://doi.org/10.1101/2021.05.20.21257484

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:

Details about study specific case and control selection criteria and how individuals were drawn from the overall iPSYCH case-cohort sample can be found in the respective publications (see below). Here we focus on differences in selection criteria in the iPSYCH cohort and additional quality control (QC) procedures.

The majority of inclusion and exclusion criteria for the original studies were also used in this study. The only difference compared to the original studies was an additional exclusion criterion that removed individuals with a moderate to severe mental retardation (ICD10: F71-F79) from both the case and control cohorts. While this criterion was also used in the original ADHD GWAS (https://www.nature.com/articles/s41588-018-0269-7), it was not used in the original ASD GWAS (https://www.nature.com/articles/s41588-019-0344-8). The rationale for this decision lies in the interpretability of our results where we treated ADHD and ASD consistently.

Wave-wise pre-imputation QC and imputation of the iPSYCH case-cohort sample were taken from the original ADHD and ASD GWAS, respectively. Details about the respective steps and filters can be found in the original GWAS publications (see above). Since our analyses

used a combined study cohort with samples from both the original ADHD and ASD GWAS, we performed some additional QC on the combined sample. Additional QC steps included the removal of related individuals across the original ADHD and ASD GWAS and a new principal component analysis (PCA) on the combined sample after exclusion of these related individuals. Following the same procedures as in the original studies, pairs of subjects were identified with pi-hat> 0.2 (using PLINK's identity-by-state analysis) and one subject of each pair was excluded at random (with a preference for keeping cases). PCA was carried out using smartPCA in the EIGENSOFT software package using the Ricopili pipeline. The original PGC datasets for ADHD and ASD did not include overlapping individuals and therefore the original datasets and summary statistics were used. The final combined dataset across all samples comprised 34,462 cases (i.e., individuals with an ADHD and/or ASD diagnosis) and 41,201 controls. We only included samples of European ancestry from the original ADHD and ASD GWAS. Among the cases in the iPSYCH cohort 11,964 had an ADHD-only, 9,315 had an ASD-only, and 2,304 individuals had a comorbid diagnosis, respectively. Thus, the proportion of ADHD among ASD cases in the iPSYCH cohort was 19.8%, and the proportion of ASD among ADHD cases was 16.1%.

File Description

asdVSadhdWOid50_filtered_clean.gz: Differentiating GWAS meta-analysis of ADHD vs ASD (11,964 ADHD cases and 9,315 ASD cases)

MD5 checksum (asdVSadhdWOid50_filtered_clean.gz) =
1a62eee19d3572ffa4981b37124961ef

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
FRQ A1 allele frequency in ADHD cases ('<' = f < 0.4 ; '<>' = 0.4 < f < 0.6; '>' = f > 0.6)
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
Neff Half effective sample size per SNP (ADHD and ASD cases)

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 Manuel Mattheisen (manuel.mattheisen@gmail.com) or Anders Børglum (anders@biomed.au.dk).

Data Use Agreement

1. Investigators acknowledge that 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;
6. Investigators will never attempt to identify any participant who contributed to these data;
7. Investigators may not use these data to develop any type of risk or predictive test for an unborn individual;
8. For any risk or predictive test for a child or adult, investigators must acknowledge that this is an experimental use of these data and that essentially all psychiatric disorders have important non-genetic etiological components;
9. When these data are made available prior to publication, investigators agree to respect and not compete with the scientific priorities of the iPSYCH team according to the Fort Lauderdale principles.

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.