Genome-Wide Association Studies of Broad Antisocial Behaviour.

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Key points

Question: Which genetic variants are associated with antisocial behaviour, are they sex-specific and do they correlate with other traits?

Findings: Genome-wide association analyses in population based studies reveal that antisocial behaviour is a highly polygenic trait, demonstrating pleiotropic genetic effects with educational attainment and distinct genetic effects across sex.

Meaning: Larger samples, split on sex, are needed to validly identify genetic variants associated with antisocial behaviour.

Abstract

IMPORTANCE: Antisocial behaviour (ASB) places a large burden on perpetrators, victims, and society as a whole. Twin studies indicate that half of the variation in this trait is genetic. Specific causal genetic variants have, however, not been identified.

OBJECTIVES: The Broad Antisocial Behaviour Consortium was set up to estimate the SNP-based heritability of ASB, to identify novel genetic risk variants, genes or biological pathways, to test for pleiotropic effects with other psychiatric traits and to re-evaluate the candidate gene era data.

DESIGN AND SETTING: Genome-wide association (GWA) data of five large population-based cohorts and three target samples with genome-wide genotype and ASB data were meta-analyzed. All datasets employed quantitative phenotypes, except for the Finnish Crime Study, that applied a case-control design (Ncases=370, Ncontrols=5850).

PARTICIPANTS: The discovery samples comprised 16,400 individuals, while the target samples consisted of 9381 individuals (all subjects were of European descent),including both child and adult samples (mean age range: 6.7-56.1 years).

MAIN OUTCOME AND MEASURES: We adopted relatively broad inclusion criteria to achieve a quantitative measure of ASB derived from multiple measures, maximizing the sample size over different age ranges.

RESULTS: Three loci approached genome-wide significance, with sex discordant effects (females, N=8535, chr1: rs2764450, chr11: rs11215217; males, N=7772, chrX, rs41456347). Polygenic risk score analyses showed prediction of antisocial phenotypes in an independent Finnish Crime Study (N=6220, Nmales=2536, Nfemales=3684) as well as shared genetic etiology with conduct problems in a population-based sample (N=825, Nmales=394, Nfemales=431), but not with conduct disorder in a substance-dependent sample (N=2336, Nmales=950, Nfemales=1386). Lastly, we detected a significant inverse genetic correlation of ASB with educational attainment (r=-.52, p=.005).

CONCLUSIONS AND RELEVANCE: The Broad Antisocial Behaviour Consortium entails the largest collaboration to date (total *N*=25,781) on the genetic architecture of antisocial behaviour and

our first results suggest that antisocial behaviour is highly polygenic and has potential heterogeneous genetic effects across sex.

Antisocial behaviour (ASB) covers a range of inappropriate behaviours that cause harm to others, the community and the environment. These include aggressive behaviour, hostility, theft, deceitfulness and violent felonies. Apart from the monetary effects[1], violent criminal behaviour also has significant social and emotional costs. Communities with high rates of crime often face high unemployment rates and high rates of drug and alcohol abuse, poverty and other social pathologies[2].Victims of crime, are often left with emotional trauma and can experience serious mental health problems, such as post-traumatic stress disorder[3]. In addition, ASB shows high co-morbidity with other psychiatric traits and maladaptive behaviours[4,5]. Against this backdrop, identifying causal mechanisms underlying ASB is critically important to identify prevention and treatment modalities. Accumulated evidence from quantitative and molecular genetic studies reveals the substantial impact of genetic factors in the etiology of ASB. The majority of evidence for a role of genetics is derived from twin studies and, to a lesser extent, adoption studies, and indicates that about half of the variance in ASB can be explained by genetic factors, whereas the remainder can be explained by unique and common environmental factors [6–8]. Twin studies further determined that the relationship between ASB and cognitive and psychiatric traits is in part due to common genetic factors, indicating there may be shared biological mechanisms underlying these behaviours[9,10]. Early candidate gene studies identified a number of genetic polymorphisms involved in serotonergic and catecholaminergic function, among others, that may be involved in ASB[9]. However, a systematic review and meta-analysis of the majority of published genetic association studies on aggression and violence failed to reveal a significant overall association between any of the previously reported candidate genes and

aggression[10]. The lack of replication of candidate genes for ASB is consistent with other candidate gene studies in psychiatry, which for the most part have failed to identify reproducible and clinically useful genetic variants[11]. This is partly due to the *a priori* inferences of the classical candidate gene approach, which increases the chances of false positive findings in the typically small sample sizes of these individual studies[12].

Genome-wide association studies (GWAS) can overcome these limitations. To date, relatively few GWAS have focused on antisocial phenotypes. One study, carried out on childhood conduct disorder in an American sample (N=3963, including 872 cases and 3091 controls), detected three genome-wide significant loci[13]. However, none of the other published GWAS studies Tielbeek et al. 2012[14] (QIMR, N=4816, continuous measure of adult antisocial behaviour), Salvatore et al. 2015[15] (COGA, N=1379, continuous measure of adult antisocial behaviour, part of the present meta-analysis), Viding et al. 2010[16] (TEDS, N=1186 (Ncases=593), psychopathic tendencies) and Derringer et al. 2015[17] (Center on Antisocial Drug Dependence, N=1901, continuous measure of behavioural disinhibition) reported evidence for a genome-wide association with any genetic variants[14–17].

This lack of positive results from GWAS is most likely due to low statistical power to detect small effects[18]. For example, recent work of the Schizophrenia Working Group of the Psychiatric Genomics Consortium (PGC) illustrated the direct relationship between sample size and success in detecting genetic variants. Their latest GWAS, including 36,989 cases and 113,075 controls, identified 108 genome-wide significant independent genomic loci, providing new insights in the pathology of schizophrenia[19], while earlier studies (2009, 2013) detected 1 and 13 genome-wide

significant SNPs, with total sample sizes of 6909 (Ncases=3322) and 59,318 (Ncases=21,246), respectively[20,21].

To increase sample sizes for gene finding for ASB, we initiated the Broad Antisocial Behaviour Consortium (BroadABC). BroadABC represents a collaborative research initiative to conduct genetic analyses on a larger scale to identify biological mechanisms underlying the course of ASB. In designing BroadABC's gene-discovery strategies, we weighed the benefits and costs of outcome measure heterogeneity in relation to the total sample size. We chose to maximize sample size by pooling the heterogeneous measures of the individual cohorts, including different age ranges, and jointly analysing their data. Our rationale is supported by genetically informative longitudinal studies demonstrating evidence for genetic continuity (the continuity in antisocial behaviour during childhood and adolescence is largely explained by genetic factors)[22]. Moreover, prior studies examining the etiological connections between the externalizing spectrum, have shown that additive genetic factors account for 81% of the variance in externalizing behaviour[23]. Lastly, previous meta-analytical GWAS studies have successfully applied this joint analysis approach, by identifying additional loci associated with depressive symptoms and neuroticism[24]. BroadABC thus focuses on the broad spectrum of ASB and currently consists of five discovery cohorts (combined, N=16,400) and three independent prediction and replication samples: i) a population-based sample, N=825; ii) a forensic sample, N=6220 iii); and a substance-dependent sample, N=2336. In total, BroadABC has genotypic and phenotypic data from 25,781 individuals across eight unique samples, making it the largest collective sample available to estimate the effects of genome wide genetic variants for ASB and testing for genetic overlap with other traits.

Materials and methods

Cohorts and phenotypes

All participants provided informed consent and local research ethics committees or institutional review boards approved the individual studies. Because of the extra perceived vulnerability of the Finnish Crime Study participants, multiple committees (Ethics Committee for Pediatrics, Adolescent Medicine and Psychiatry, Hospital District of Helsinki and Uusimaa, and Criminal Sanctions agency) approved this study[25]. Except for the Finnish Crime Study, which used a dichotomized outcome measure, all studies employed a continuous scale to increase statistical power[26]. To maximize sample size, we included studies with a broad range of antisocial measures, including both aggressive and non-aggressive domains of ASB, and utilizing study-specific scales in different age groups (see Table 1 and Supplementary Information, Chapter 1). Five large population-based discovery cohorts and three target samples (all subjects were of European descent) were included in this study (see Table 1 for cohort-specific details). The discovery samples comprised 16,400 individuals, while the target samples consisted of 9381 individuals. All participants were recruited from different regions, thus making sample overlap highly unlikely.

Genotyping

Genome-wide genotyping was performed independently in the cohorts using commercially available genotyping arrays. All cohorts imputed their genotype data to the 1000 Genomes phase 1 version 3 (build 37, hg19) reference panel using the standard software package MACH[27]

or IMPUTE2[28], except for the Finnish Crime Study and MSUTR, which were not imputed. Additional details and cohort-specific procedures concerning the genotyping process, imputation, and quality control are provided in the Supplementary Information, Chapter 2 and Table S1).

Statistical analyses

GWAS at cohort level

Genome-wide association analyses (GWA) were performed at the cohort level according to a pre-specified analysis plan (Standard Operating Procedures; SOP). Each cohort uploaded sex-specific and combined GWAS results to the BroadABC server as input for the meta-analyses. All analyses were restricted to samples of European ancestry. For sex-pooled analysis of the X chromosome, males were treated as homozygous females. Quality control (QC) and meta-analysis of the GWA summary results were performed by two independent analysts (J.J.T. & A.J.), following a strict analysis protocol. Further details on the SOP analysis plan and QC are provided in the Supplementary Information (Chapter 3) and on the website of BroadABC, http://broadabc.ctglab.nl/.

Meta-analysis of discovery cohorts

The meta-analysis across discovery cohorts was run for the pooled male-female GWAS results (N=16,400), as well as separately for the sexes (females, N=8535; males, N=7772), using a fixed-effects model with z-scores weighted by sample size as implemented in the software METAL[29]. We only reported and interpreted the results of polymorphisms with a total sample size greater than 10,000 (across all samples) and 5000 (sex-specific). The genome-wide significance

threshold was set at 1.67×10^{-8} as we performed three meta-analyses and polymorphisms with p-values $< 10^{-6}$ were considered suggestive findings.

Polygenic risk scores

We performed a polygenic risk score (PRS) analysis in the Finnish Crime Study to test whether a genetic risk for ASB could significantly discriminate between prisoners and matched controls. We used the software package PRSice to estimate the best-fit PRS at a broad range of p-value thresholds. For clumping, the LD threshold was set to an r^2 of .25 and 500 kb distance. PRS analyses were conducted based on the sex-combined samples and the male-specific samples (given the overrepresentation of male prisoners) and sex, age, and four principal components were included as covariates. In addition, to evaluate evidence for shared genetic etiology, we employed the summary-summary statistic based analysis as implemented in PRSice, using the sex-combined, male-specific and female-specific samples in MSUTR and Yale-Penn, after applying more stringent clumping thresholds (r^2=.05, 300 kb distance).

LD regression score heritability and correlation analyses

To calculate the SNP heritability and estimate the genetic correlation between ASB and a range of cognitive, psychiatric and reproductive traits, we used the (cross-trait) LD score regression method. The LD score method disentangles the contribution of true polygenic signal and bias due to population stratification to the inflated test statistics in GWAS, and optionally calculates a genetic correlation (r_g) between different traits [30]. This method is particularly useful since it only requires GWAS summary statistics and is not biased by sample overlap[31]. Genetic correlations of ASB were calculated with cognitive and psychiatric traits, previously reported to be co morbid with ASB, using summary results from ADHD, schizophrenia and bipolar disorder [19,32,33] that are

publicly available on the Psychiatric Genomics Consortium (PGC) webpage (https://www.med.unc.edu/pgc/results-and-downloads, accessed 5 September 2015). The summary statistics of neuroticism and educational attainment (defined as 'number of years in the educational system') were provided by the Social Science Genetic Association Consortium [24,34]. The genetic correlations of ASB with reproductive traits were computed from a centralized database of summary-level GWAS (LDHUB)[35].

The Methods and Results section regarding the functional annotation, gene analysis, gene-set analyses, replication analysis and tests for enrichment in loci previously related to antisocial phenotypes are reported in the Supplementary Information (Chapter 4, 5, 6, 7; Table S3, S4 and Figure S5).

Results

We removed 2,134,049 SNPs due to insufficient total sample size (N < 10 000), resulting in 7,392,849 SNPs available for analyses. There were no discrepancies between the results files of the two analysts at either the cohort level or the meta-analysis level. The genomic inflation factors for the combined, male and female meta-analyses were 1.015, 1.012 and 1.001, respectively, which are as expected under a polygenic model given the current sample size, prevalence, and heritability of ASB (see QQ-plots Figure S2A).

Meta-analysis of GWAS

The combined discovery meta-analysis, incorporating both sexes, did not identify genetic variants of genome-wide significance (N=16,400, lowest p= 6.1×10^{-7}). The strongest associations were located on chromosome 20, followed by chromosomes 1, 19, 22 and 6 (see Manhattan plot, Figure S1A). SNPs yielding p values smaller than p= 1.0×10^{-6} were considered to be suggestive (Table S2a).

The GWAS meta-analysis for females only (N=8535, Table S2b) revealed three loci approaching genome-wide significance on chromosome 1 (rs2764450, $p= 4.8 \times 10^{-8}$, R^2=.35%) and 11 (rs11215217, $p= 2.1 \times 10^{-8}$, R^2=.37%), whereas the meta-analysis for males (N=7772, Table S2c) identified a near genome-wide signal on chromosome X (rs41456347, $p= 2.0 \times 10^{-8}$, R^2=.41%). We found no evidence for heterogeneity (I^2=0) across discovery samples in the association of rs2764450 (p=.45), rs11215217 (p=.54) and rs41456347 (p=.60) with ASB (see Figure S4 for forest plots). Functional annotation was carried out for the top three loci to gain insight into possible causal genes (see Chapter 7 and Figure S5). Top signals were located differently across sex, which is illustrated by the Miami plot in Figure 1 and Table S5. We tested whether the signs of the regression coefficients were consistently in the same direction between the SNPs for males and females. The sign tests showed no consistent directions of effect (proportion was .51, .50 and .50 respectively) for SNPs selected for different p-value thresholds (.05, .001 and .0001). Moreover, Fisher exact tests showed no evidence for enrichment of SNPs with low p-values across sex, regardless of sign (odds ratio was .9 and 1.1 for p-values .05 and .001 respectively, for more details and the number of SNPs per test, see Table S6).

The sex-specific signals were supported by a large number of suggestive SNPs, which were in incomplete LD with the lead SNP (See regional association plots, Figure S1B). Imputation quality for the lead SNPs was high (average r^2 = 99.7, 93.8 and 86.8) for rs41456347, rs2764450 and rs11215217, respectively. Gene-based and gene-set analyses yielded no significant genes (top gene= *CENPI*, $p= 3.2 \times 10^{-5}$, Table S3a-c, Figure S3) or gene-sets (top gene-set=*'Reactome cell communication'*, $p= 3.6 \times 10^{-4}$, Table S3d). None of the traditional candidate genes on antisocial behaviour were significantly associated with ASB (top gene=TH, p_{corr}=.0841, Table S4a-c).

Polygenic risk scores

The BroadABC antisocial genetic risk scores could predict case-control status of antisocial personality disorder in the Finnish Crime Study (sex-combined, p=.031; male-specific, p=.05, in the most optimal model, see Figure 2A and 2B). Nevertheless, the analyses revealed low Nagelkerke's R^2 estimates (R^2=.0019 in the most optimal model) not exceeding the Bonferroni corrected threshold for significance. Using summary statistics in PRsice software, we found that the genetic effect from the females-only ASB analysis significantly overlapped with genetic effects in the expected direction on conduct problems in MSUTR (p= .004, R^2=.021 for the most optimal model, see Figure 2E), but not with the sex-combined and males-only analyses (Figure 2C and 2D). No significant genetic overlap was found with conduct disorder in YalePenn, although a nominal significant effect (p=.04, R^2=.0022) in the expected direction was found in the males-only analysis (Figure 2E, 2F and 2G).

SNP heritability and genetic correlation of ASB with other traits

The estimated proportion of the phenotypic variance in ASB explained by all SNPs was 5.2% with a standard error of 2.7% (p<.05). Sample sizes were too small in the sex-specific meta-analyses to be used to estimate SNP h^2 for the male and female samples separately. We found a significant (corrected α=.006) and moderate negative genetic correlation between ASB and educational attainment (r=-.52, p=.005). Follow-up analyses, utilizing Fisher's exact test, showed evidence of enrichment of low P (p-values below the threshold p<.001) in same SNPs for ASB

and educational attainment (OR=3.26, p=.001). Moreover, we found a suggestive positive genetic correlation with neuroticism (r=.29, p=.02) and support for a negative genetic correlation between ASB and Age at Menopause (r=-.49, p=.01), Age of First Birth (r=-.43, p=.008) and a positive genetic correlation with Number of Children Ever Born (r=.42, p=.03), see Table 2. There was no evidence for genetic overlap between ASB and Schizophrenia, Bipolar Disorder, ADHD or Age at Menarche.

Discussion

This study represents the largest (N=25,781) investigation on the genetic architecture of antisocial behaviour to date. Our meta-analyses of diverse continuous measures of ASB showed that ASB is heritable and highly polygenic and suggests that part of the genetic architecture is sex specific. This is not surprising in view of the sex-influenced phenotypic expression. We also found a strong inverse correlation of ASB with genetic variants for educational attainment and some reproductive traits, and a positive genetic correlation with neuroticism, but not with schizophrenia, bipolar disorder, or ADHD.

SNP heritability analyses demonstrated that the collective effect of the measured SNPs accounted for 5% of the variance, or 10% of the heritability of ~50%, as estimated from family-based studies. Recent GWAs on other complex traits such as height, BMI, and schizophrenia clearly demonstrated that with greater sample sizes the SNP h^2 increases. The relatively small total GWAS discovery sample size (N=16,400), yielded limited power to detect small genetic effects which could partly explain the high "missing heritability" in our study, although we cannot rule out that most of the genetic variance in ASB is due to rare alleles. Taken together, we suspect that with greater sample sizes and better imputation and coverage of both the

common and rare allele spectrum, over time, SNP heritability in ASB could approach the family-based estimates.

Polygenic risk score analysis, based on a broad conceptualization of ASB, could reliably predict some of the variation in antisocial personality disorder in a forensic cohort, demonstrating that population-based genetic association studies can also be informative for samples that are at-risk. Nevertheless, effect sizes were very small, indicating limited prediction accuracy and clinical utility for the current GWAS outcomes.

Despite the small but significant collective genetic effect on ASB, none of the individual genetic variants exceeded the significance threshold in our overall meta-analysis. The sex-specific meta-analyses, however, revealed three loci approaching genome-wide significance. Moreover, stronger polygenic risk effects were found for the sex-specific analyses. Given the substantial differences in prevalence, age of onset, and severity of ASB between males and females [36], which might partly reflect sex differences in genetic architecture, it is important to account for those effects in genetic research designs[37]. Our current results suggest the presence of at least partly sex-specific genetic effects. Even though sample sizes were smaller, the sex-specific analyses yielded increased specificity because potential noise, due to different genetic loci driving the genetic component of ASB in males and females, was removed.

Our genetic correlation analyses revealed a suggestive positive genetic correlation of ASB with neuroticism, which is concordant with previous twin research demonstrating a shared genetic etiology of externalizing behaviour and negative emotionality[38]. Moreover, we found significant genetic overlap between ASB and educational attainment, indicating a common underlying

362 genetic architecture influencing both phenotypes. The negative genetic correlation with
363 educational attainment is consistent with previous epidemiological studies reporting a negative
364 association between academic performance and delinquency[39]. This finding is important, as it
365 may shed some light on the developmental pathways that underlie the relationship between
366 academic failure and ASB[40]. Strikingly, ASB also correlates with reproductive traits, thus fitting to
367 the unified evolutionary theory that Boutwell and others proposed [41]. Their theory suggests that
368 increased criminality represents a faster life history approach, one that would be significantly
369 calibrated by genes.
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371 *Conclusions*
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373 As large-scale initiatives, such as the Broad Antisocial Behaviour Consortium, continue to grow,
374 these collaborative efforts will also facilitate the conduct of epidemiologic studies that
375 incorporate genome-wide data and environmental factors in a joint analysis[43]. Discoveries
376 obtained from such gene-environment-wide interaction studies may contribute to more
377 advanced explanatory models of the complex etiology of antisocial behaviour, thereby
378 ultimately aiding prevention and intervention strategies[44].
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Table 1. Study design, sample sizes and phenotypes for GWAS cohorts.

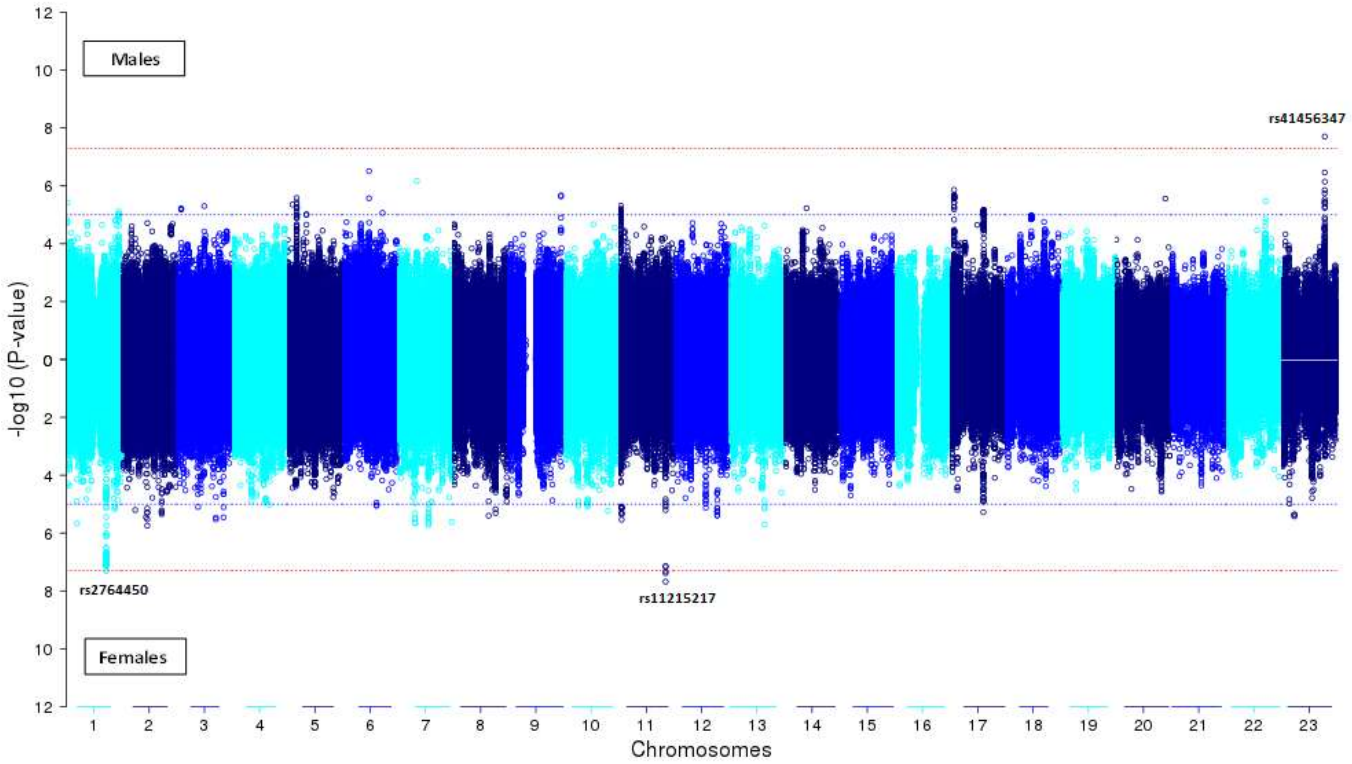
Sample	Study design	Antisocial measure	Sample size *N*(♂/♀)	Mean age (SD)
Discovery samples				
ALSPAC	Prospective pregnancy cohort (family design)	Development and Wellbeing Assessment (DAWBA), conduct disorder scale	4336 (2065/2271)	13.1 (.1)
COGA	Alcohol dependence case-control sample (family design)	Count of the number of Antisocial Personality Disorder criteria (ASPD)	1379 (739/640)	43.8 (11.7)
GENR	Population-based (family design)	Rule-breaking behaviour, Teacher Report Form (TRF)	1420 (718/702)	6.7 (4.2)
TEDS	Population-based (family design)	Antisocial Process Screening Device (APSD)	2734 (1257/1477)	12.5 (.2)
QIMR	Population-based (twin-family design)	Retrospective Conduct Disorder (SSAGA-Oz)	6531 (2993/3538)	33.8 (2.4)
Target samples				
Finnish Crime Study	Case-control (prisoners sample)	The Structured Clinical Interview For DSM-IV-Disorders (SCID)	6220 (2536/3684)	56.1 (12.8)
MSUTR	Population-based (family design)	Child Behavioral Checklist (CBCL): Conduct Problems (Reported by mother)	825 (394/431)	8.2 (1.5)
Yale-Penn	Substance-dependent sample	DSM-IV Conduct Disorder criteria	2336(950/1386)	41.0 (8.2)

ALSPAC= Avon Longitudinal Study of Parents and Children, COGA= Collaborative Studies on Genetics of Alcoholism, GENR= Generation Rotterdam, TEDS= The Twins Early Development Study, QIMR = Queensland Institute of Medical Research, MSUTR = Michigan State University Twin Registry.

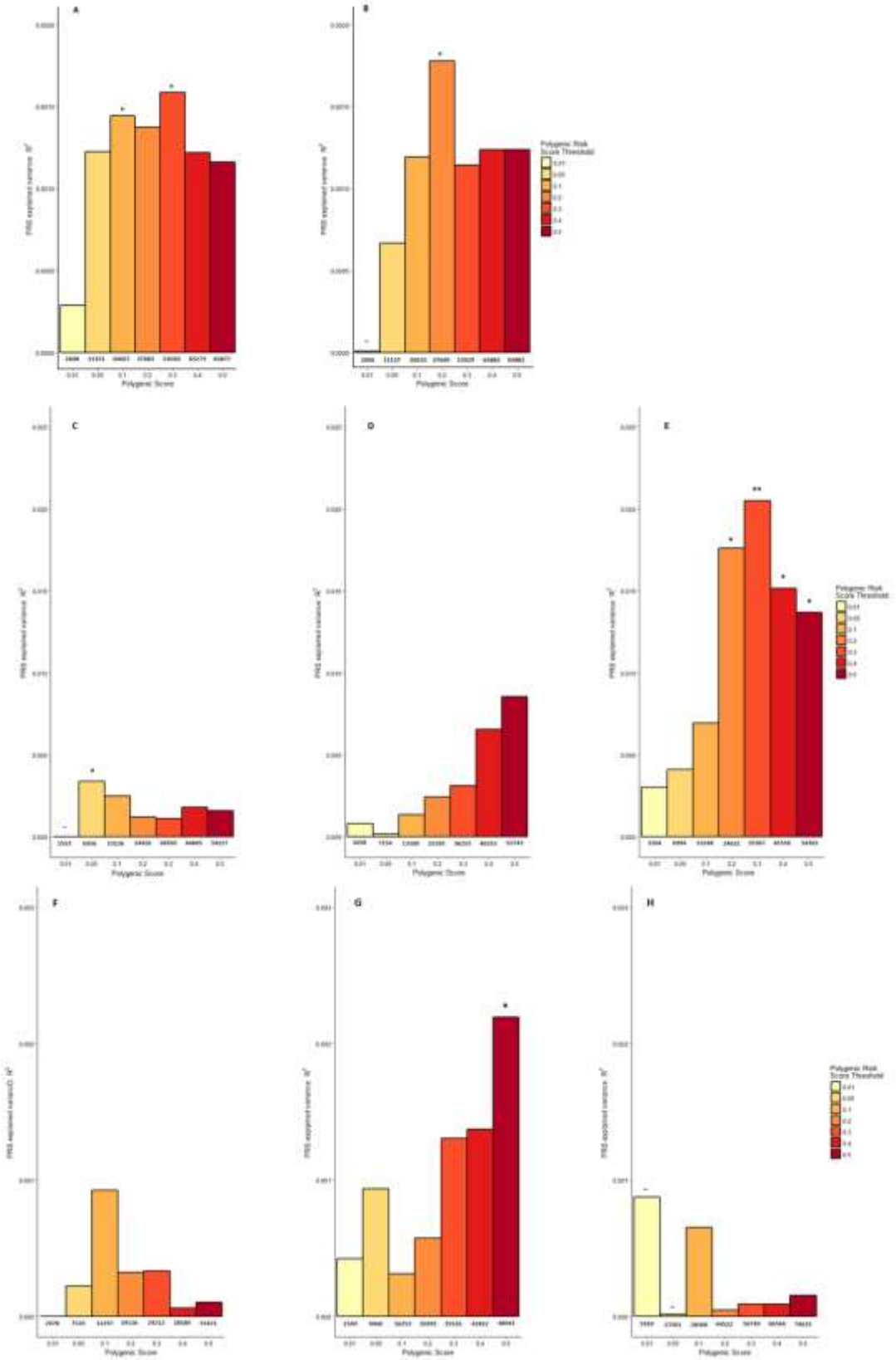
Table 2. Genetic correlation estimates for nine different traits with broad antisocial behaviour.

Phenotype	***Sample size***	***SNP h2***	***r_g(SE)***	***P-value***
Educational attainment	293,723	.099	-.52 (.18)	.005
Neuroticism	170,911	.094	.29 (.13)	.02
Schizophrenia	150,064	.576	.07 (.15)	.64
Bipolar Disorder	17,091	.516	.17 (.20)	.41
Attention Deficit Hyperactivity Disorder	9152	.156	.002 (.29)	.99
Age at Menarche	87,802	0.207	-0.04 (.09)	0.68
Age at Menopause	69,360	0.134	-0.49 (.19)	0.010
Age of first birth	251,151	0.061	-0.43 (.16)	0.008
Number of children ever born	343,072	0.025	0.42 (.19)	0.03

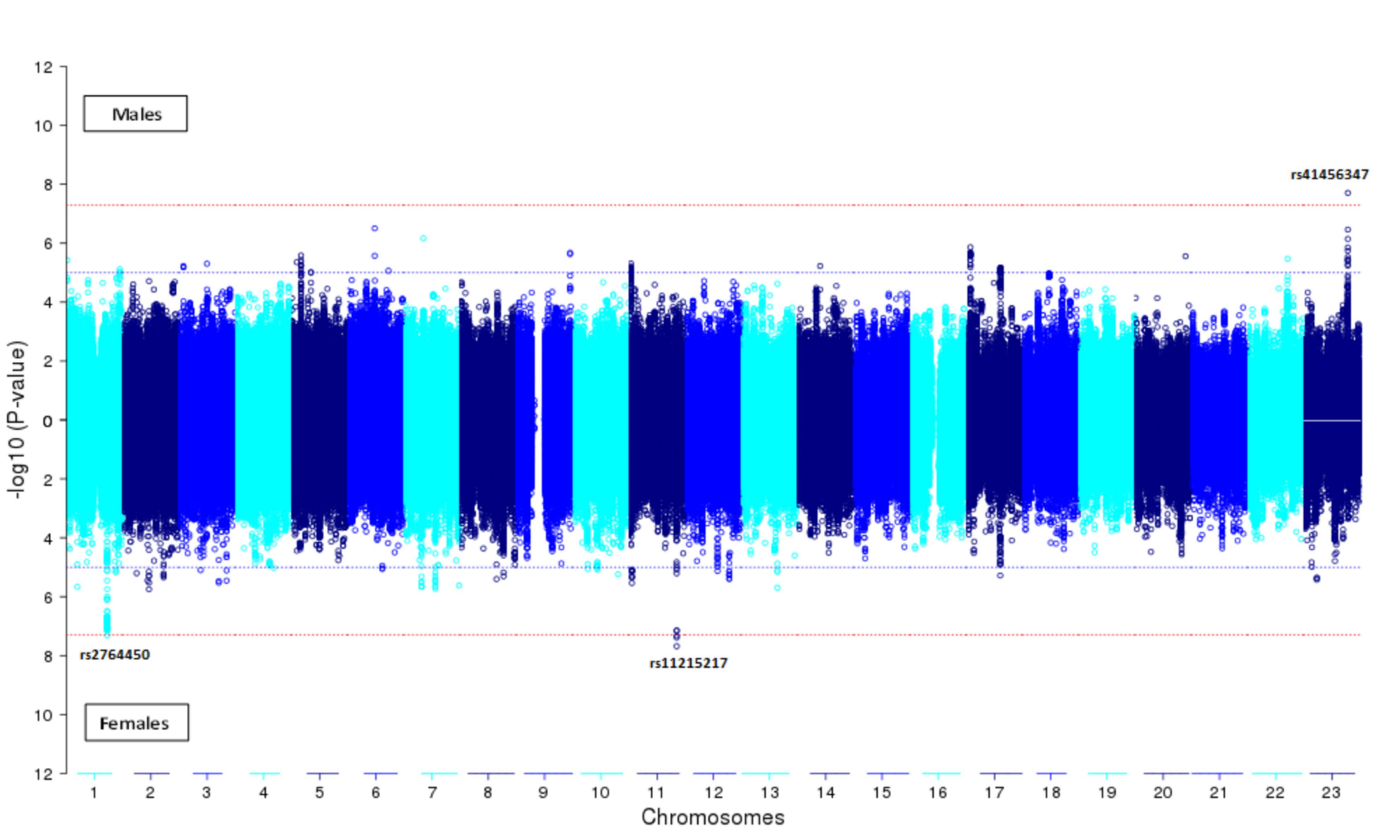
Note: Nominally significant (p<.05); Significant at the multiple-testing corrected p-value (.006). GWAS summary statistics from our sex-combined analyses were used to calculate the r_g's with other traits. SNP h^2 is the estimation of narrow-sense heritability. r_g is the genetic correlation and is calculated with the LDSC software package using pre-calculated LD scores from Finucane et al.[45].

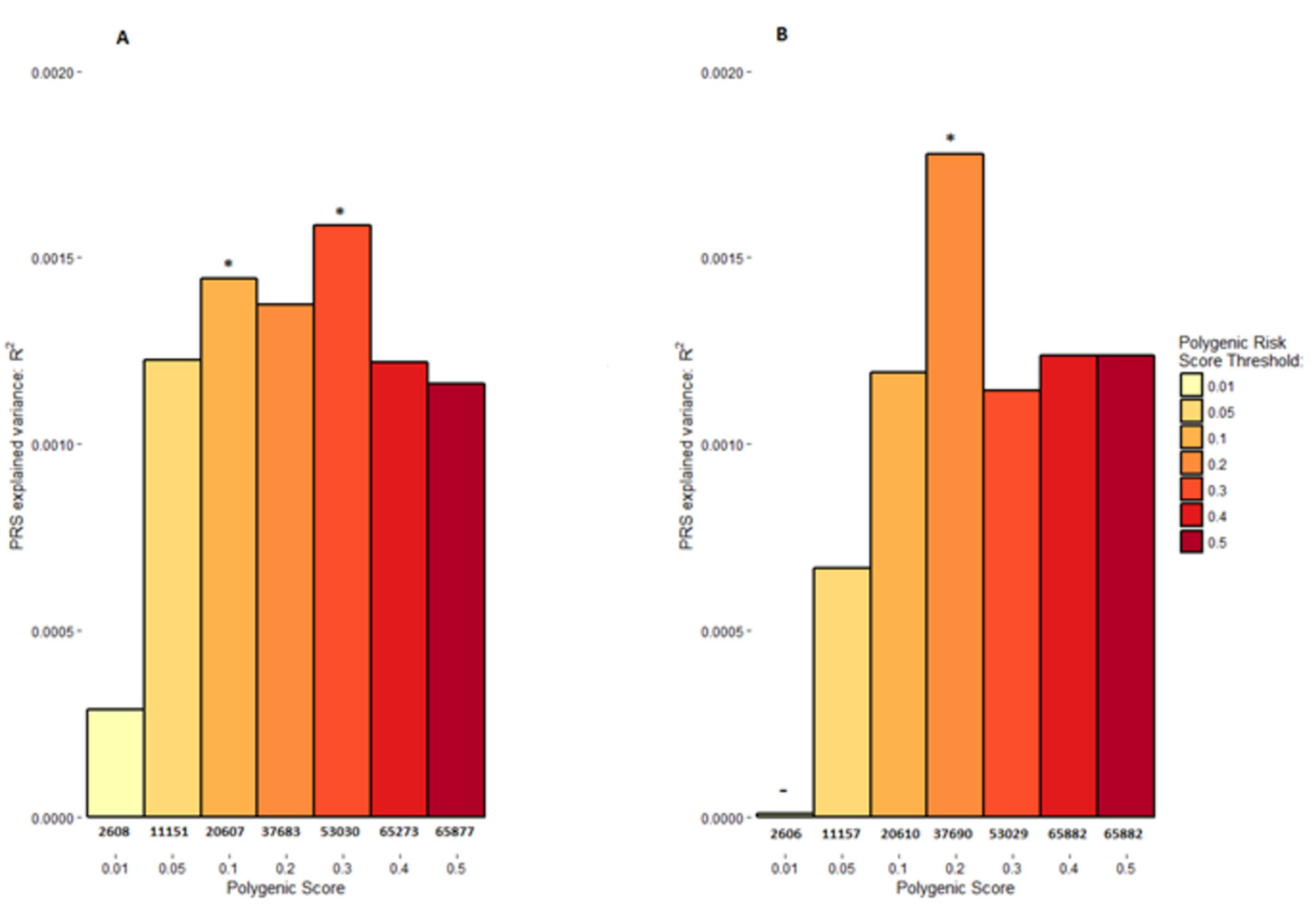


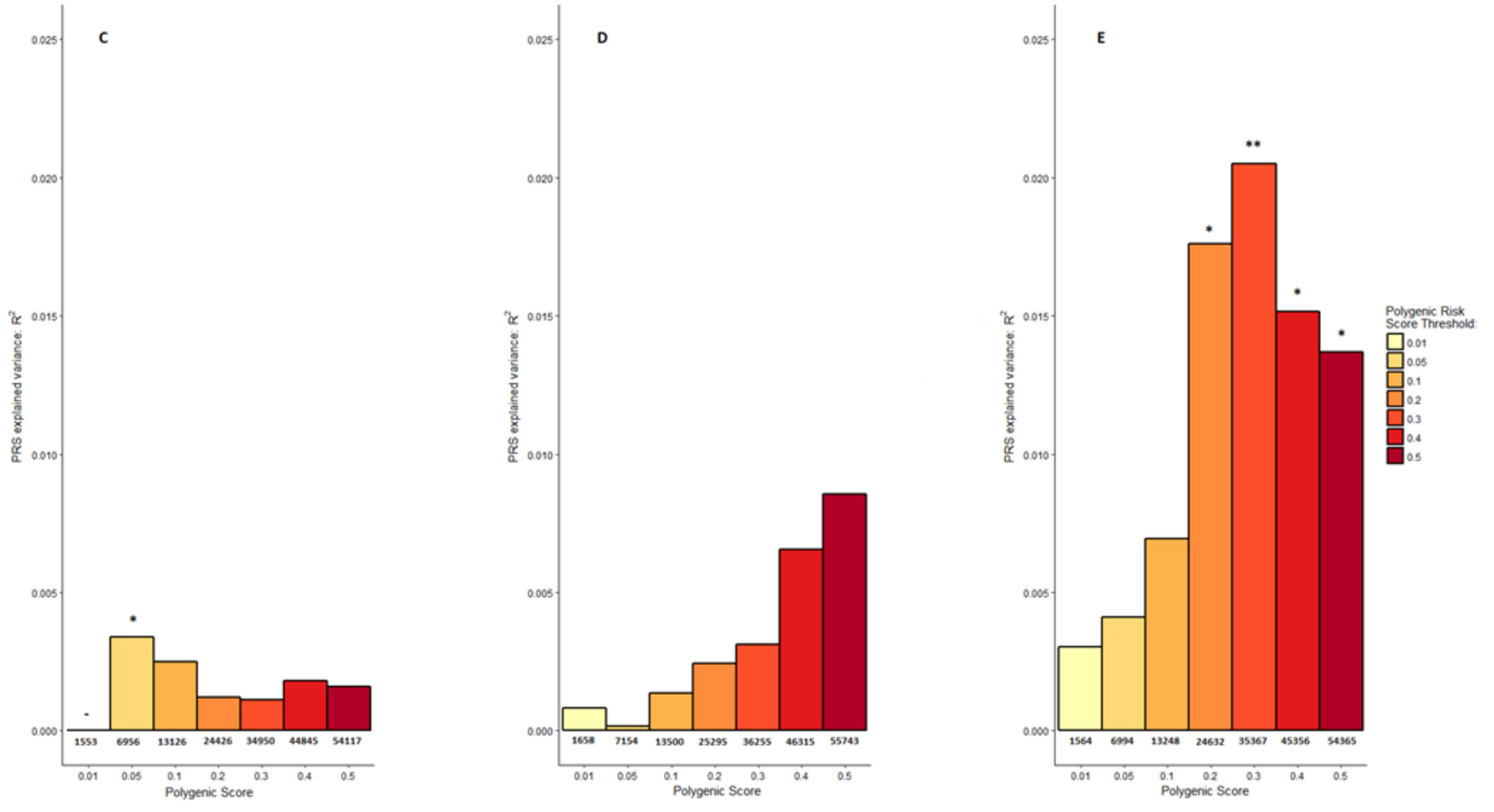
The threshold for genome-wide significance (P < 1.67 ×10-8) is indicated by the red dotted line and the threshold for suggestive significance (P < 1.0 ×10-5) is indicated by the blue dotted line.

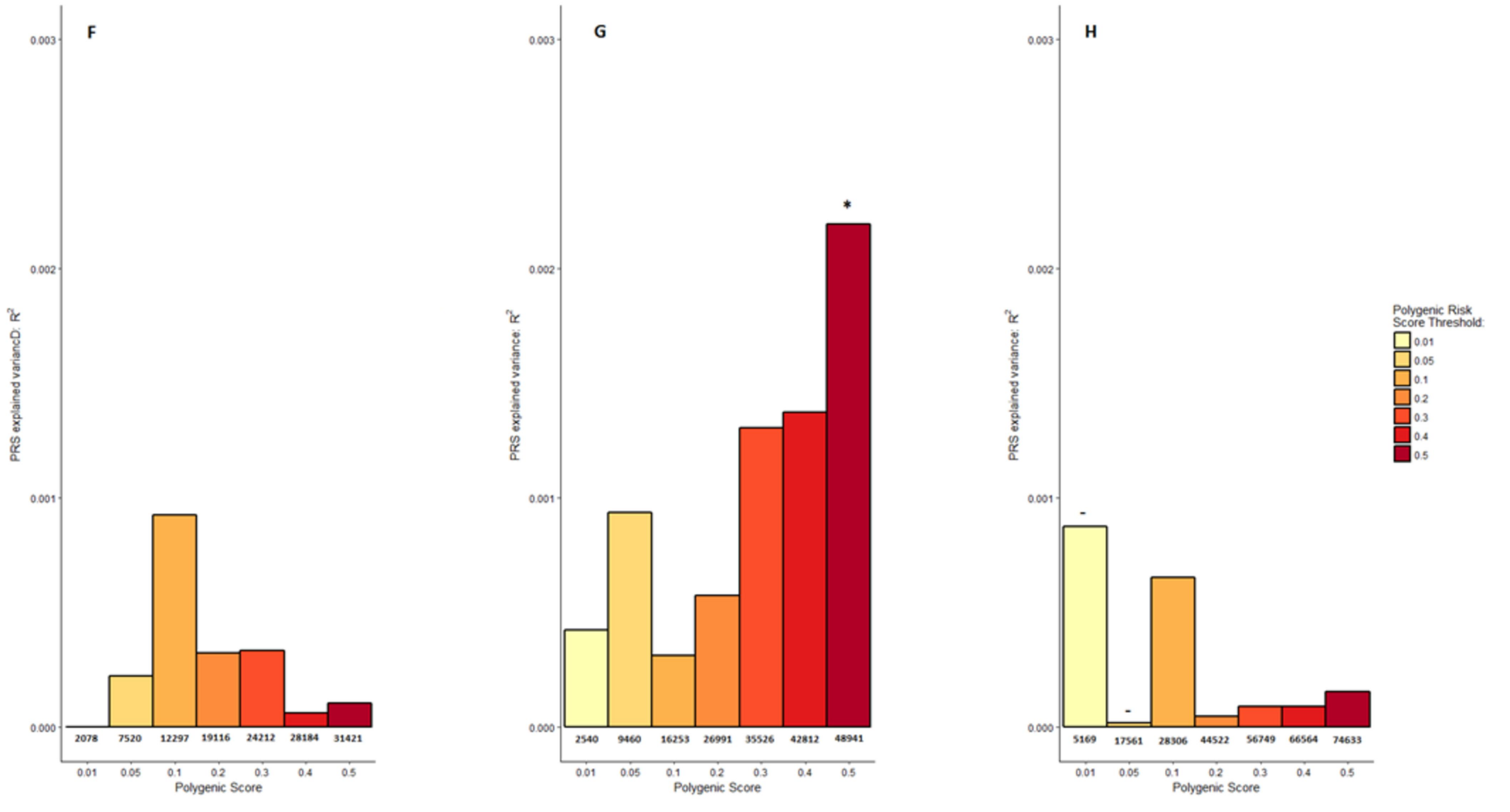


Polygenic risk scores computed with the PRSice software package for broad antisocial behaviour predicting antisocial personality disorder (ASPD) in the Finnish Crime Study using sex-combined (A) and males-only (B) samples. Summary-summary statistic based results of PRSice software package plotting the explained variance in ASB within MSUTR (sex-combined (C), males-only (D) and females-only (E)) and Yale-Penn (sex-combined (F), males-only (G) and females-only (H)). The proportion of variance explained (Y-axis; Nagelkerke's R2) was computed by comparison of a full model (covariates + PRS) score to a reduced model (covariates only). Seven different p-value thresholds for selecting risk alleles are denoted by the colour of each bar. The number of SNPs per threshold is displayed below each bar. Asterisks (*) indicate nominal significant (p<.05) prediction.


Males
Females
rs41456347
rs2764450
rs11215217
-log10 (P-value)
Chromosomes
12
10
8
6
4
2
0
2
4
6
8
10
12
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23


A
B
PRS explained variance: R^2
Polygenic Score
0.01
0.05
0.1
0.2
0.3
0.4
0.5
2608
11151
20607
37683
53030
65273
65877
2606
11157
20610
37690
53029
65882
65882
Polygenic Risk Score Threshold:


C
D
E
PRS explained variance: R^2
Polygenic Score
1553
6956
13126
24426
34950
44845
54117
1658
7154
13500
25295
36255
46315
55743
1564
6994
13248
24632
35367
45356
54365
Polygenic Risk Score Threshold:


F
G
H
PRS explained variance: R^2
Polygenic Score
2078
7520
12297
19116
24212
28184
31421
2540
9460
16253
26991
35526
42812
48941
5169
17561
28306
44522
56749
66564
74633
Polygenic Risk Score Threshold: