PGCASDEuro_Mar2015.readme

URL: http://www.med.unc.edu/pgc/files/resultfiles/pgcasdeuro.gz
Source: Autism Spectrum Disorder Working Group of the Psychiatry Genomics Consortium
Publication Status: intermediate data release – no associated publication
Notes: This data reflects an early analysis from the ASD-PGC working group – a more up to data version is expected to be published in Q1 2017
Citation: For all studies that use any of these data please site the following;
Autism Spectrum Disorder Working Group of the Psychiatry Genomics Consortium. Dataset: PGC-ASD summary statistics from a meta-analysis of 5,305 ASD-diagnosed cases and 5,305 pseudocontrols of European descent (based on similarity to CEPH reference genotypes) (March 2015). (available at: http://www.med.unc.edu/pgc/results-and-downloads)

File Description

Filename: PGC.ASD.euro.all.25Mar2015.txt
Size: 553,795,981

SNP	Marker Name
CHR	Chromosome
BP	Location (hg19)
A1	reference allele for OR (may not be minor allele)
A2	alternate allele
OR	OR (with respect to A1)
SE	SE to OR
P	Association Test (P-value)
INFO	Imputation quality score
EUR_FRQ	Allele Frequency in EUR dataset (not verified – may include errors / discard)

Introduction

This is the result files from the first PGC Autism mega-analysis (http://pgc.unc.edu).

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 appropriate PGC publication in any communications or publications arising directly or indirectly from these data.

Methods.

Participating Studies

The discovery sample consists of genomewide genotyping data from five studies. Genotype data was available on parent-parent-proband trios; Sample sizes (N) refer to number of probands and derived pseudocontrols; the Geschwind Autism Center of Excellence (ACE; N = 391/391), the Autism Genome Project (AGP; N = 2272/2272 probands [1,2]), the Autism Genetic Resource Exchange (AGRE; N = 974/974 [3,4], the NIMH Repository, the Montreal/Boston Collection (MONBOS; N = 1396/1396 [5]), and the Simons Simplex Collection (SSC; N = 2231/2231 [6]).

Diagnostic Classification

For each of the individuals included in the mega-analysis, an ASD diagnosis was confirmed by the contributing sites using research standard diagnoses and expert clinical consensus diagnosis. Additional summary statistics from diagnostic instruments, including the Autism Diagnostic Interview-Revised (ADI-R) or the Autism Diagnostic Observation Schedule (ADOS) were available on 94.1% of individuals examined in this study. Individuals were excluded from the analyses if they were assessed at less than 36 months old or if there was any evidence of the diagnostic criteria not being met on either the ADI-R or ADOS.

Genotyping

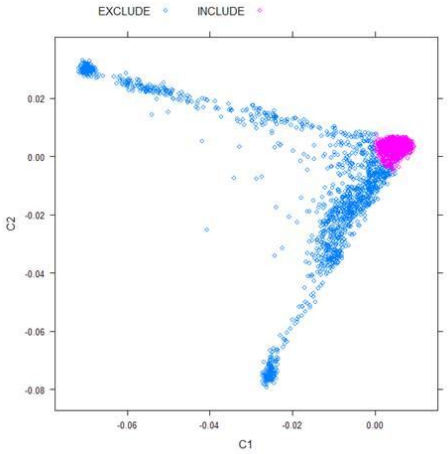
Whole genome SNP genotyping was performed using a range of genotyping platforms including the Affymetrix 500K (AGRE, NIMH), Affymetrix 5.0 (AGRE, NIMH, MONBOS), the Illumina 550 (AGRE), Illumina 1M single (AGP, SSC), Illumina 1M Duo (AGP, SSC), Illumina 2.5M Omni (ACE, SSC). Genotyping procedures for individual studies are described elsewhere [1,2,5-8].

To limit study and array biases, quality control, imputation and association analyses were performed separately for each consortium dataset in which a different genotyping array was used. The parameters for retaining SNPs and individuals were: SNP missingness (prior to subject removal) < 0.05; subject missingness < 0.02; autosomal heterozygosity deviation F_{het} < 0.2; Mendel-errors per individual < 10,000; SNP missingness (post subject removal) < 0.02; SNP Hardy Weinberg deviation in founders ($P > 10^{-6}$), SNP Mendel-errors < 4.

The parent–proband trios were converted to a proband–pseudocontrol study design prior to imputation. After phasing of the trio, the pseudocontrol is a simulated individual derived from the untransmitted parental alleles. For any SNP, the pseudocontrols are the 3 genotypes that could have been formed by the parental alleles, but were not transmitted to the proband: for parents with genotypes a_1a_2 and a_3a_4 and offspring a_1a_3, pseudocontrols are a_1a_4, a_2a_3 and a_2a_4. Here one pseudocontrol, a_2a_4 was retained for analysis. In multi-offspring families each affected offspring was converted in such a proband-pseudocontrol pair.

All imputation was performed using IMPUTE2 with pre-phasing of haplotypes performed using SHAPEIT [9-11]. SNP array data was aligned to the reference strand and imputed against the 1000 genomes project phase 1 integrated reference haplotypes (December 2013; http://mathgen.stats.ox.ac.uk/impute/data_download_1000G_phase1_integrated_SHAPEIT2_9-12-13.html). Following imputation, SNPs with imputation quality (INFO >0.4) were retained for further analyses.

Ancestry Definition



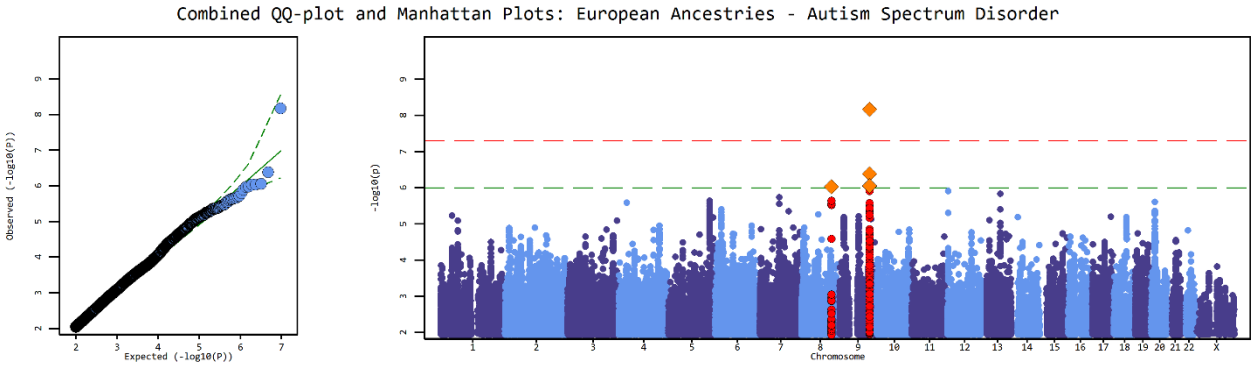
A total of 6495 individuals with ASD met inclusion criteria and had genomewide SNP data available. Each of these individuals were from parent-proband trio collections and included genomewide SNP data from both parents. To identify a more genetically homogenous set of individuals, we calculated the Euclidean distance for each sample along the top 3 principal components (PCs) from the combined CEU and TSI HapMap reference populations. The Euclidean distances were weighted by variance explained for each of the top 3 PCs; i.e. 2 x PC1, 1 x PC2, 0.15 x PC3. Individuals that were greater than 10 standard deviations from the reference mean were excluded, yielding 5,305 individuals denoted "G1"; The G1 population is broadly considered to be of European Caucasian ancestry.

Genetic Association Analyses

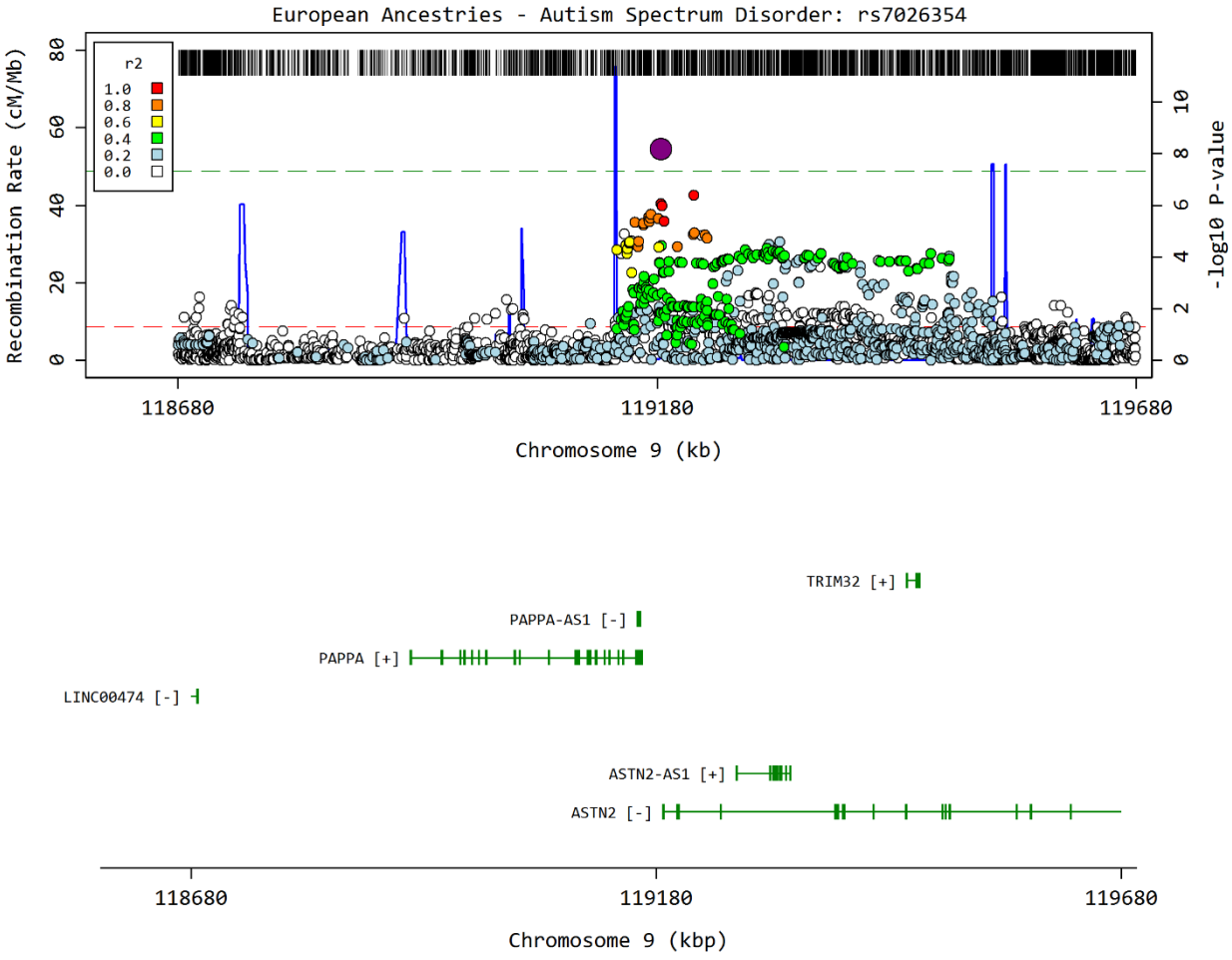
All autosomal association analyses was performed using the --assoc routine in PLINK v1.08p using the imputed dosage genotypes. The unsuitability of dosage data for the non-PAR region of the X-chromosome constrained those analyses to "best guess" genotypes. Analyses included only cases who met criteria and their matched pseudo-control. Meta-analysis of genomewide association scans was performed using the inverse-variance based meta-analysis routine in METAL [12]. Following meta-analyses, the parameters for retaining SNPs were minor allele frequency greater than 1% and imputation unsuccessful in no more than one subset. Subsequently, quality control limited these analyses to approximately 9.7 million markers. All summary statistics will be available freely for public download at http://www.med.unc.edu/pgc/downloads. Regional association plot creation for these data are freely available at http://www.broadinstitute.org/mpg/ricopili/ .

Results

Combined QQ and Manhattan Plot for European (G1) subsets with Autism Spectrum Disorder Diagnosis



Regional association plot for the marker rs7026354 in the European Ancestries - Autism Spectrum Disorder genome scan. SNPs showing correlation to the index SNP was defined using the clump flag in PLINK 1.9a beta (available at; https://www.cog-genomics.org/plink2/; build: 8th April 2014). Linkage dependence is defined as SNPs within a 1MB window showing correlation (r2) > 0.2. Linkage disequilibrium was calculated using the reference genotypes from European subset of phase 1 v3.0 1000 genomes project (available at; https://mathgen.stats.ox.ac.uk/impute/data_download_1000G_phase1_integrated.html). Extended transcripts are plotted using co-ordinates reported in the refGene file (ftp://hgdownload.cse.ucsc.edu/goldenPath/hg19/database/refGene.txt.gz; download 12Jan2015). All regional association plots created using the self-authored program locus_plot.ado implemented in STATA13 (StataCorp, USA).



Summary of linkage disequilibrium independent SNPs showing association at P < 10-5 for the Autism Group Psychiatric Genomics Consortium European Ancestry G1 ASD subset (N = 5305). All gene-co-ordinates refers to chromosome an hg19 genome reference position. Allele refers to the index allele, genotype and observed frequencey for ASD (FRQ_A) and pseudo-control (FRQ_U). Odd Ratio refers to effect size and 95% confidence interval). Genes refers to transcripts which overlap the region of association as defined by LD Range; transcripts are assigned using co-ordinates reported in the refGene file (ftp://hgdownload.cse.ucsc.edu/goldenPath/hg19/database/refGene.txt.gz; download 12Jan2015).

Marker	SNP Location	Associated Region	Allele (GT;FRQ_A:FRQ_U)	Association		Gene in Region
				Odds Ratio (95%CI)	P-value	
rs7026354	9:119184126	9:119138164-119485270	A (A:G; 0.476:0.436)	1.17 (1.11-1.24)	6.70E-09	ASTN2 ASTN2-AS1 PAPPA PAPPA-AS1 TRIM32
rs7836146	8:119095022	8:119094919-119104103	A (A:C; 0.202:0.230)	0.85 (0.79-0.91)	9.16E-07	EXT1
rs66847009	12:3982482	12:3890095-4001019	T (T:C; 0.084:0.103)	0.79 (0.71-0.87)	1.07E-06	PARP11
rs112096205	13:70915010	13:70903001-70951805	A (A:G; 0.089:0.071)	1.28 (1.16-1.42)	1.29E-06	NONE
rs1088553	7:77947894	7:77862252-77953248	T (T:C; 0.603:0.634)	0.87 (0.82-0.92)	1.60E-06	MAGI2
rs9285005	5:163586122	5:163549613-163647529	A (A:G; 0.122:0.141)	0.80 (0.73-0.88)	2.02E-06	NONE
rs6079556	20:14745223	20:14696882-14914709	A (A:C; 0.428:0.461)	0.88 (0.83-0.93)	2.18E-06	MACROD2 MACROD2-AS1
rs187962005	4:31820379	4:31820379-31820379	A (A:C; 0.040:0.050)	0.64 (0.53-0.77)	2.28E-06	NONE
rs142968358	6:23819235	6:23667424-23906447	T (T:G; 0.558:0.527)	1.14 (1.08-1.21)	3.43E-06	NONE
rs78927543	7:114625789	7:114614284-114715717	T (T:G; 0.024:0.035)	0.67 (0.57-0.80)	3.93E-06	MDFIC
rs192259652	20:14842867	20:14842867-14907661	A (A:T; 0.839:0.858)	0.81 (0.74-0.89)	4.25E-06	MACROD2 MACROD2-AS1
rs1513723	8:66703788	8:66679221-66755163	C (C:G; 0.384:0.414)	0.88 (0.83-0.93)	4.74E-06	PDE7A
rs79857083	1:44283497	1:43955148-44294920	T (T:C; 0.602:0.573)	1.15 (1.08-1.21)	5.11E-06	KDM4A KDM4A-AS1 LOC101929592 PTPRF ST3GAL3
rs73503170	9:76190694	9:75881358-76200815	A (A:G; 0.808:0.832)	0.85 (0.79-0.91)	5.44E-06	NONE
rs77422917	17:73521599	17:73246961-73521599	A (A:C; 0.270:0.244)	1.16 (1.09-1.24)	5.46E-06	CASKIN2 GGA3 GRB2 KIAA0195 LOC100287042 MIF4GD MIR3678 MIR6785 MRPS7 SLC25A19 TSEN54
rs34426491	14:20293131	14:20293131-20302493	A (A:G; 0.050:0.060)	0.66 (0.55-0.79)	5.64E-06	OR4N2
rs75764795	9:16857335	9:16836723-16886487	T (T:C; 0.103:0.085)	1.25 (1.13-1.37)	5.64E-06	BNC2
rs9962572	18:49675410	18:49670828-49701229	T (T:G; 0.809:0.832)	0.84 (0.79-0.91)	5.66E-06	NONE
rs4958993	5:177371713	5:177371713-177371713	A (A:G; 0.017:0.024)	0.52 (0.39-0.69)	5.85E-06	NONE
rs72767788	9:124971170	9:124971170-124980130	A (A:C; 0.825:0.847)	0.84 (0.78-0.91)	6.41E-06	LHX6
rs190797148	13:27837510	13:27668253-27866392	C (C:G; 0.021:0.031)	0.64 (0.53-0.78)	6.90E-06	LINC00412 RASL11A RPL21 RPL21P28 SNORA27 SNORD102 USP12 USP12-AS1 USP12-AS2

rs2312573	1:67172148	1:66984125-67219536	A (A:T; 0.292:0.320)	0.87 (0.82-0.93)	7.05E-06	MIR3117 SGIP1 TCTEX1D1
rs183016945	3:196056756	3:196056756-196056756	T (T:C; 0.964:0.955)	1.53 (1.27-1.84)	7.07E-06	TM4SF19 TM4SF19- TCTEX1D2
rs7449665	6:144122363	6:144103420-144154911	A (A:G; 0.129:0.150)	0.84 (0.77-0.90)	9.80E-06	PHACTR2
rs2005582	4:160318744	4:160181374-160355746	A (A:G; 0.399:0.429)	0.88 (0.84-0.93)	9.86E-06	RAPGEF2

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References

1 Anney, R. *et al.* A genome-wide scan for common alleles affecting risk for autism. *Hum Mol Genet* **19**, 4072-4082, doi:10.1093/hmg/ddq307 (2010).
2 Anney, R. *et al.* Individual common variants exert weak effects on the risk for autism spectrum disorders. *Hum Mol Genet* **21**, 4781-4792, doi:10.1093/hmg/dds301 (2012).
3 Lajonchere, C. M. & Consortium, A. Changing the landscape of autism research: the autism genetic resource exchange. *Neuron* **68**, 187-191, doi:10.1016/j.neuron.2010.10.009 (2010).
4 Geschwind, D. H. *et al.* The autism genetic resource exchange: a resource for the study of autism and related neuropsychiatric conditions. *Am J Hum Genet* **69**, 463-466, doi:10.1086/321292 (2001).
5 Weiss, L. A., Arking, D. E., Daly, M. J. & Chakravarti, A. A genome-wide linkage and association scan reveals novel loci for autism. *Nature* **461**, 802-808, doi:nature08490 [pii]
10.1038/nature08490 (2009).
6 Chaste, P. *et al.* A genomewide association study of autism using the Simons Simplex Collection: Does reducing phenotypic heterogeneity in autism increase genetic homogeneity? *Biological Psychiatry* **Advanced Online (29th September)** (2014).
7 Wang, K. *et al.* Common genetic variants on 5p14.1 associate with autism spectrum disorders. *Nature* **459**, 528-533, doi:nature07999 [pii]
10.1038/nature07999 (2009).
8 Ma, D. *et al.* A genome-wide association study of autism reveals a common novel risk locus at 5p14.1. *Annals of human genetics* **73**, 263-273, doi:10.1111/j.1469-1809.2009.00523.x (2009).
9 Howie, B. N., Donnelly, P. & Marchini, J. A flexible and accurate genotype imputation method for the next generation of genome-wide association studies. *PLoS Genet* **5**, e1000529, doi:10.1371/journal.pgen.1000529 (2009).
10 Howie, B., Fuchsberger, C., Stephens, M., Marchini, J. & Abecasis, G. R. Fast and accurate genotype imputation in genome-wide association studies through pre-phasing. *Nat Genet* **44**, 955-959, doi:10.1038/ng.2354 (2012).
11 Delaneau, O., Marchini, J. & Zagury, J. F. A linear complexity phasing method for thousands of genomes. *Nat Methods* **9**, 179-181, doi:10.1038/nmeth.1785 (2012).
12 Willer, C. J., Li, Y. & Abecasis, G. R. METAL: fast and efficient meta-analysis of genomewide association scans. *Bioinformatics* **26**, 2190-2191, doi:10.1093/bioinformatics/btq340 (2010).