The Penetrance of Copy Number Variations for Schizophrenia and Developmental Delay

Supplemental Information

Table S1. Summary of the new samples of cases and controls analyzed for the current study. For analysis of CNVs in this study we only used SNPs that were overlapping on all these arrays:

Dataset	Source (accession ID)	Array (*n* probes)	*n* Samples Before QC	*n* Samples After QC
Schizophrenia Batch 1	Broad Institute	HumanOmniExpress-12v1 (730,525)	2,469	2,393
Schizophrenia Batch 2	Broad Institute	HumanOmniExpressExome-8v1 (951,117)	3,621	3,490
Schizophrenia Batch 3	Broad Institute	HumanOmniExpressExome-8v1 (951,117)	1,039	999
The Genetic Architecture of Smoking and Smoking Cessation	dbGaP (phs000404.v1.p1)	Illumina HumanOmni2.5 (2,443,179)	1,491	1,488
High Density SNP Association Analysis of Melanoma: Case-Control and Outcomes Investigation	dbGaP (phs000187.v1.p1)	Illumina HumanOmni1_Quad_v1-0-B (1,051,295)	3,102	2,971
Genetic Epidemiology of Refractive Error in the KORA Study	dbGaP (phs000303.v1.p1)	Illumina HumanOmni2.5 (2,443,179)	1,869	1,857
WTCCC2 samples from National Blood Donors (NBS) Cohort	EGA (EGAD00000000024)	Illumina 1.2M (1,238,733)	2,697	2,375
WTCCC2 samples from 1958 British Birth Cohort	EGA (EGAD00000000022)	Illumina 1.2M (1,238,733)	2,921	2,564

CNV, copy number variation; NBS, National Blood Service; QC, quality control; SNP, single nucleotide polymorphism; WTCCC, Wellcome Trust Case Control Consortium.

Copy Number Variation (CNV) Calling and Quality Control (QC)

Genotyping of the schizophrenia (SCZ) patients from the CLOZUK and CardiffCOGS samples was performed at the Stanley Center for Psychiatric Research at the Broad Institute, Cambridge, Massachusetts on two different arrays: HumanOmniExpress-12v1 (Omni Express array), and HumanOmniExpressExome-8v1 (Combo array) (Table S1). The Combo array contains, in addition to the single nucleotide polymorphisms (SNPs) from the Omni Express, those from the Illumina HumanExome-12v1_A (Exome array). Different Illumina array platforms were used for genotyping the case and control datasets, each with different SNP probe sets (Table S1). To make the CNV calling comparable across the different arrays used, we only analyzed the 520,766 probes present on all arrays on Table S1. A CNV was called as covering a CNV locus if it spanned >50% of the region commonly accepted for that CNV (Table S2). In the case of loci that include only single genes (*NRXN1, SIM1, YWHAE, PAFAH1B1* and *NF1*), we accepted CNVs that intersected at least one exon of the gene in question.

Each case and control dataset was analyzed independently to avoid batch effects. The raw intensity data was processed using the Illumina Genome Studio software (v2011.1). PennCNV (http://www.openbioinformatics.org/penncnv/) was used to call CNVs from the data following the standard protocol and adjusting for GC content. Samples were excluded if for any one of the following QC metrics they represented an outlier in their source dataset: Log2 ratio standard deviation, B-allele frequency drift, wave factor and total number of CNVs called per person. The proportion of excluded samples in the control datasets should not be taken as evidence about different quality of the datasets, as some of these had already been filtered for quality before being downloaded from dbGaP. Samples were checked for duplicates with an identity by descent analysis using PLINK (pngu.mgh.harvard.edu/~purcell/plink/) and the duplicate with the better QC was retained. After the poorly performing and duplicated samples had been identified and excluded, all CNVs went through further QC filtering. Firstly, raw CNVs in the same sample were joined together if the distance separating them was less than 50% of their combined length, using an in-house developed program freely available from http://x004.psycm.uwcm.ac.uk/~dobril/. CNVs were then excluded if they were covered by less than 10 probes, were less than 10 kb in length, overlapped with low copy repeats by more than 50% of their length, or had a probe density (calculated by dividing the size

of the CNV by the number of probes covering it) greater than 20 k. The remaining high quality CNVs from each dataset were then merged together and CNV loci with a frequency greater than 1% were filtered out using PLINK.

The remaining rare CNVs were required to pass a median Z-score outlier method of validation freely available from http://x004.psycm.uwcm.ac.uk/~dobril/. This method is detailed in Kirov *et al*., 2012 (15). Briefly, the Z-score method standardizes SNP probe intensities for each individual across all SNP probes and then standardizes the intensity of each SNP probe across all individuals. These rounds of standardization help reduce noise created by natural fluctuations in probe intensity. A median Z-score value for all standardized probe intensities within a putative CNV region is used to assess copy number, with true deletions and duplications represented as outliers in the samples median Z-score distribution. Z-score histograms of CNVs with marginal Z-Scores (between -6 to -4 and +2 to +4) were visually inspected using the Illumina GenomeStudio v2011.1 software.

The MGS and ISC samples were genotyped at the Broad Institute, Cambridge, Massachusetts, using Affymetrix 6.0 genotyping arrays (for MGS) and Affymetrix 6.0 or 5.0 (for ISC). CNVs were called using the Birdsuite algorithm, and filtered for size (<15 kb) and probe cover (<15 probes). Similar criteria as above were used for joining CNVs, filtering for low copy repeats (LCRs), 50% cover of CNV loci, 1% frequency criterion, Log2 ratio standard deviation, and total number of CNVs called per person (as an outlier of the distribution in the dataset). For the purpose of this analysis we retained all ethnicities from all datasets. Restricting the data to only white European subjects makes practically no difference to the conclusions (data not shown), as the frequencies of most of these CNVs are under strong selection pressure and are not governed by the laws of genetic drift, in the way common variants are, and because the subjects with an European origin make up the vast majority of the samples: >91% of the "Current study" samples listed in Table S1, all of the ISC and a substantial proportion of the MGS sample (2,671 cases and 2,648 controls), while the remaining samples in that dataset are of African American ancestry.

Table S2. Rate of CNVs in different phenotypes.

Locus	Position	*n* probes on Illumina Arrays	MR/DD/CM/ASD	SCZ	Controls
1p36 del	chr1:0,00-10,07	1954	0.24% (78/32,587) A	0% (0/13,465) D	0% (0/17,873) D
1q21.1 del	chr1:146,57-147,39	223	0.29% (97/33,226) B	0.17% (33/19,056) E	0.021% (17/81,821) E
1q21.1 dup	chr1:146,57-147,39	223	0.2% (68/33,226) B	0.13% (21/16,244) E	0.037 (24/64,046) E
NRXN1 del	chr2:50,14-51,26	236	0.18% (12/6,623) C	0.18% (33/18,759) F	0.02% (10/51,161) F
2q23.1 del	chr2:148,72-149,29	47	0.06% (20/32,587) A	0.0074% (1/13,465) D	0% (0/17,873) D
2q37 del	chr2:239,71-242,47	622	0.052% (17/32,587) A	0% (0/13,465) D	0% (0/17,873) D
2q37 dup	chr2:239,71-242,47	622	0.006% (2/32,587) A	0% (0/13,465) D	0% (0/17,873) D
3q29 del	chr3:195,73-197,34	294	0.06% (20/32,587) A	0.082% (14/17,005) E	0.0014% (1/69,965) E
3q29 dup	chr3:195,73-197,34	294	0.055% (18/32,587) A	0% (0/13,465) D	0% (0/17,873) D
Wolf-Hirschhorn del	chr4:1,53-2,03	50	0.052% (17/32,587) A	0% (0/13,465) D	0% (0/17,873) D
Wolf-Hirschhorn dup	chr4:1,53-2,03	50	0.012% (4/32,587) A	0% (0/13,465) D	0% (0/17,873) D
Sotos syndrome del	chr5:175,72-177,06	256	0.043% (14/32,587) A	0% (0/13,465) D	0% (0/17,873) D
Sotos syndrome dup	chr5:175,72-177,06	256	0.012% (4/32,587) A	0.0074% (1/13,465) D	0% (0/17,873) D
6p25 del	chr6:0,16-6,06	1597	0.071% (23/32,587) A	0% (0/13,465) D	0% (0/17,873) D
6p25 dup	chr6:0,16-6,06	1597	0.037% (12/32,587) A	0% (0/13,465) D	0% (0/17,873) D
6q16 (SIM1) del	chr6:100,84-100,91	15	0.0042% (1/23,380) A	0% (0/13,465) D	0% (0/17,873) D
6q16 (SIM1) dup	chr6:100,84-100,91	15	0.0042% (1/23,380) A	0% (0/13,465) D	0.0056% (1/17,873) D
WBS del	chr7:72,74-74,14	207	0.25% (83/32,587) A	0% (0/13,465) D	0% (0/17,873) D
WBS dup	chr7:72,74-74,14	207	0.12% (39/32,587) A	0.066% (14/21,269) G	0.0058% (2/34,455) G
8p23.1 del	chr8:8,09-11,89	1056	0.055% (18/32,587) A	0.0074% (1/13,465) D	0% (0/17,873) D
8p23.1 dup	chr8:8,09-11,89	1056	0.074% (24/32,587) A	0% (0/13,465) D	0% (0/17,873) D
9q34 del	chr9:137,81-141,08	657	0.055% (18/32,587) A	0% (0/13,465) D	0% (0/17,873) D
9q34 dup	chr9:137,81-141,08	657	0.025% (8/32,587) A	0% (0/13,465) D	0% (0/17,873) D
10q23 del	chr10:81,96-88,80	1344	0.086% (28/32,587) A	0% (0/13,465) D	0% (0/17,873) D
10q23 dup	chr10:81,96-88,80	1344	0.015% (5/32,587) A	0.015% (2/13,465) D	0% (0/17,873) D
15q11.2 del	chr15:22,80-23,09	76	0.80% (203/25113) B	0.59% (116/19,547) E	0.28% (227/81,802) E
15q11-13 (PWS/AS) any del	chr15:24,82-28,43	886	0.18% (60/32,587) A	0% (0/13,465) D	0% (0/17,873) D
15q11-13 (PWS/AS) any dup	chr15:24,82-28,43	886	0.25% (82/32,587) A	0.079 (12/15,266) E	0.0083 (5/60,148) E
15q13.3 del	chr15:31,13-32,48	235	0.26% (85/32,587) A	0.14% (26/18,571) E	0.019% (15/80,422) E

Locus	Position	*n* probes on Illumina Arrays	MR/DD/CM/ASD	SCZ	Controls
15q13.3 dup	chr15:31,13-32,48	235	0.083% (27/32,587) A	0.074% (10/13,465) D	0.039% (7/17,873) D
15q13.3 smaller (CHRNA7) del	chr15:32,01-32,45	64	0.03% (7/23,380) A	0.015% (2/13,465) D	0% (0/17,873) D
15q13.3 smaller (CHRNA7) dup	chr15:32,01-32,45	64	0.56% (130/23,380) A	0.62% (83/13,465) D	0.73% (131/17,873) D
15q24 del	chr15:72,91-74,41	196	0.025% (8/32,587) A	0% (0/13,465) D	0% (0/17,873) D
15q24 dup	chr15:72,91-74,41	196	0.012% (4/32,587) A	0% (0/13,465) D	0% (0/17,873) D
15q24.2q24.5 del	chr15:75,97-78,20	218	0.015% (5/32,587) A	0% (0/13,465) D	0% (0/17,873) D
15q24.2q24.5 dup	chr15:75,97-78,20	218	0.018% (6/32,587) A	0% (0/13,465) D	0% (0/17,873) D
15q25 del	chr15:83,18-84,74	227	0.0086% (2/23,380) A	0% (0/13,465) D	0% (0/17,873) D
15q25 dup	chr15:83,18-84,74	227	0.017% (4/23,380) A	0% (0/13,465) D	0% (0/17,873) D
16p13.11 del	chr16:15,51-16,30	358	0.15% 50/33,226 B	0.074% (10/13,465) D	0.039% (7/17,873) D
16p13.11 dup	chr16:15,51-16,30	358	0.3% (98/32,587) A	0.31% (37/12,029) E	0.13% (93/69,289) E
16p11.2p12.1 del	chr16:21,53-29,10	1462	0.061% (20/32,587) A	0% (0/13,465) D	0% (0/17,873) D
16p11.2p12.1 dup	chr16:21,53-29,10	1462	0.043% (14/32,587) A	0% (0/13,465) D	0% (0/17,873) D
16p12.1 del	chr16:21,94-22,46	67	0.19% (62/33,226) B	0.18% (24/13,465) D	0.05% (9/17,873) D
16p12.1 dup	chr16:21,94-22,46	67	0.049% (16/32,587) A	0.037% (5/13,465) D	0.05% (9/17,873) D
16p11.2 distal del	chr16:28,82-29,05	39	0.14% (46/33,226) B	0.063% (13/20,732) H	0.018% (5/27,045) H
16p11.2 distal dup	chr16:28,82-29,05	39	0.075% (25/33,226) B	0.037% (5/13,465) D	0.056% (10/17,873) D
16p11.2 del	chr16:29,64-30,20	99	0.19% (62/33,226) B	0.03% (5/16,772) E	0.041% (26/63,068) E
16p11.2 dup	chr16:29,64-30,20	99	0.28% (93/33,226) B	0.35% (58/16,772) E	0.03% (19/63,068) E
Rubinstein-Taybi del	chr16:3,78-3,93	21	0.031% (10/32,587) A	0% (0/13,465) D	0.0056% (1/17,873) D
17p13.3 (YWHAE) del	chr17:1,25-1,30	11	0.021% (7/32,587) A	0% (0/13,465) D	0.0056% (1/17,873) D
17p13.3 (YWHAE) dup	chr17:1,25-1,30	11	0.04% (13/32,587) A	0.022% (3/13,465) D	0.017% (3/17,873) D
17p13.3 (PAFAH1B1) del	chr17:2,49-2,59	14	0.025% (8/32,587) A	0% (0/13,465) D	0% (0/17,873) D
17p13.3 (PAFAH1B1) dup	chr17:2,49-2,59	14	0.028% (9/32,587) A	0% (0/13,465) D	0.0056% (1/17,873) D
Smith-Magenis (del)	chr17:16,82-18,28	284	0.095% (31/32,587) A	0% (0/13,465) D	0% (0/17,873) D
Potocki-Lupski (dup)	chr17:16,82-18,28	284	0.077% (25/32,587) A	0.0074% (1/13,465) D	0% (0/17,873) D
NF1 del	chr17:29,10-30,28	188	0.08% (26/32,587) A	0% (0/13,465) D	0.0056% (1/17,873) D
NF1 dup	chr17:29,10-30,28	188	0.11% (35/32,587) A	0.0074% (1/13,465) D	0% (0/17,873) D
17q12 del	chr17:34,81-36,20	304	0.087% (29/33,226) B	0.036% (5/14,024) E	0.0054% (4/74,447) E
17q12 dup	chr17:34,81-36,20	304	0.11% (37/33,226) B	0.045% (6/13,465) D	0.022% (4/17,873) D
17q21.31 del	chr17:43,70-44,18	78	0.13% (42/32,587) A	0% (0/13,465) D	0% (0/17,873) D

Locus	Position	*n* probes on Illumina Arrays	MR/DD/CM/ASD	SCZ	Controls
17q21.31 dup	chr17:43,70-44,18	78	0.015% (5/32,587) A	0.0074% (1/13,465) D	0% (0/17,873) D
17q23 del	chr17:58,25-60,29	256	0.018% (6/32,587) A	0% (0/13,465) D	0% (0/17,873) D
17q23 dup	chr17:58,25-60,29	256	0.0031% (1/32,587) A	0% (0/13,465) D	0% (0/17,873) D
19p13.12 del	chr19:13,08-16,70	939	0.04% (13/32,587) A	0% (0/13,465) D	0% (0/17,873) D
22q11.21 del (VCFS)	chr22:19,02-20,26	351	0.54% (175/32,587) A	0.29% (56/19,084) E	0% (0/77,055) E
22q11.21 dup	chr22:19,02-20,26	351	0.3% (136/48,637) B	0.019% (3/15,583) E	0.075% (25/33,449) E
22q11.2 distal del	chr22:21,91-23,65	283	0.11% (26/23,380) A	0% (0/13,465) D	0% (0/17,873) D
22q11.2 distal dup	chr22:21,91-23,65	283	0.077% (18/23,380) A	0.0074% (1/13,465) D	0.017% (3/17,873) D
Phelan-McDermid del	chr22:43,00-51,16	2368	0.25% (59/32,587) A	0% (0/13,465) D	0% (0/17,873) D
22q13 dup	chr22:43,00-51,16	2368	0.0092% (3/32,587) A	0% (0/13,465) D	0% (0/17,873) D

ASD, autism spectrum disorders; CM, congenital malformations; CNV, copy number variations; DD, developmental delay; del, deletion; dup, duplication; MR, mental retardation; SCZ, schizophrenia.

The numbers of CNVs and the size of the samples are given in the following format: (number of carriers/total number of tested individuals). They are taken from the following sources:

A) Girirajan *et al.*, 2012 (1): 32,587 or 23,380 cases affected with DD/ASD/CM.

B) Rosenfeld *et al.*, 2012 (2): 25,113, 33,226 or 48,637 cases affected with DD/ASD/CM.

C) Chen *et al.*, 2013 (3): 6,623cases affected with neurodevelopmental disorders.

D) Current sample (6882 cases / 11,255 controls, as presented in Table S1) + ISC study (3391 cases / 3181 controls) + MGS study (3192 cases / 3437 controls) = 13,465 cases and 17,873 controls.

E) Current sample as in D but without WTCCC controls (6882 cases / 6316 controls) + results from the review by Malhotra & Sebat (4) (various numbers). The WTCCC controls were included in most of the estimates in the other reviews, including that of Malhotra & Sebat (4), therefore they are not included in the "current sample" numbers in these and in the remaining loci listed below.

F) For *NRXN1*: Current sample as in D), but without WTCCC controls (6882 cases / 6316 controls) + review by Kirov *et al.*, 2009 (ref 13 from the main text) + MGS study as reported by Levinson *et al.* (68).

G) For WBS: Current sample as in D) but without WTCCC controls (6882 cases / 6316 controls) + results by Mulle *et al.* (69).

H) For 16p11.2 distal deletion: Current sample as in D) but without WTCCC controls (6882 cases / 6316 controls) + results by Guha *et al.* (50).

"*n* probes on Illumina arrays" refers to the number of probes common on all Illumina arrays used in the "Current sample" that cover the CNV regions presented in this table, column 2.

Table S3. Publications used to derive the *de novo* rate and selection coefficients of CNVs. The table lists the disorders on which the observations were made. The numbers are presented as *de novo*/(*de novo*+inherited). The selection coefficients (*s*) are presented in the last two columns, as the ratio of *de novo*/(*de novo*+inherited) numbers. No selection coefficients are presented for cases with <5 observations, as they would be very unreliable. The list of CNVs is based on Girirajan *et al.* (1) and for most loci that are not associated with SCZ, the numbers are based on that paper alone. In bold are results for loci associated with SCZ.

Locus	Reference	Deletions	Duplications
1p36	Girirajan *et al.* (2012) (1)	**9/11=0.82**	NA
1q21.1	Brunetti-Pierri *et al.* (2008) (5): MR/AU/physical anomalies	3/17	1/12
	Mefford *et al.* (2008) (6): MR	8/17	3/5
	Buysse *et al.* (2009) (7): MR	2/3	0/1
	Jaillard *et al.* (2010) (8): MR	0/1	-
	Christiansen *et al.* (2004) (9): CHD	1/2	-
	Malhotra *et al.* (2011) (10): BD, SCZ	**-**	0/2
	Griswold *et al.* (2012) (11): ASD	**-**	1/2
	Rosenfeld *et al.* (2012) (2): DD/CM/ASD	7/39	5/30
	Girirajan *et al.* (2013) (12): ASD	0/1	4/8
	Total:	**21/80=0.26**	**14/60=0.23**
2p16.3 (*NRXN1*) exonic del	Guilmatre *et al.* (2009) (13): ASD/MR	0/3	NA
	Glessner *et al.* (2009) (14): ASD	0/7	
	Kirov *et al.* (2012) (15): SCZ	0/3	
	Bradley *et al.* (2001) (16): ADHD	1/1	
	The Autism Genome Project Consortium (2007) (17): ASD	1/1	
	Ching *et al.* (2010) (18): variable phenotypes	4/11	
	Shen *et al.* (2010) (19): ASD	0/1	
	Bremer *et al.* (2011) (20): ASD	0/1	
	Sanders *et al.*/Levy *et al.* (2011) (21, 22): ASD	1/4	
	Schaaf, *et al.* (2012) (23): DD	3/12	
	Total:	**10/44=0.23**	
2q23.1	Girirajan *et al.* (2012) (1): DD/ASD/CM	1/2	NA
2q37	Girirajan *et al.* (2012) (1): DD/ASD/CM	2/3	0/2
3q29	Ballif *et al.* (2008) (24): MR	5/8	2/10
	Willatt *et al.* (2005) (25): variable phenotypes	5/5	-
	Mulle *et al.* (2010) (26): SCZ	1/1 del	-

Locus	Reference	Deletions	Duplications
	Kirov *et al.* (2012) (15): SCZ	1/1 del	-
	Bremer *et al.* (2011) (20): ASD	1/1	-
	Sanders *et al.*/Levy *et al.* (2011) (21, 22): ASD	1/1	-
	Malhotra *et al.* (2011) (4): BD	1/1	-
	Girirajan *et al.* (2011) (27): DD/AU/Dyslexia	1/1del	1/1dup
	Girirajan *et al.* (2012) (1): DD/ASD/CM	3/4del	0/8dup
	Total:	**19/23=0.83**	3/19=0.16
Wolf-Hirschhorn syndrome	Girirajan *et al.* (2012) (1): DD/ASD/CM	1/2	1/1
Sotos syndrome	Girirajan *et al.* (2012) (1): DD/ASD/CM	1/1	0/1
6p25	Girirajan *et al.* (2012) (1): DD/ASD/CM	1/13=0.08	0/6=0
6q16	Girirajan *et al.* (2012) (1): DD/ASD/CM	-	0/1
WBS	Sanders *et al.* (2011) (22): AU	-	4/4
	Van der Aa *et al*. (2009) (28): MR	-	5/12
	Girirajan *et al*. (2011) (27): DD/AU/Dyslexia	1/1	-
	Dixit *et al*. (2013) (29): DD/ASD/CM	-	4/5
	Mulle *et al*. (in press): SCZ	-	2/2
	Griswold *et al*. (2012) (11): ASD	-	0/1
	Girirajan *et al*. (2012) (1): DD/ASD/CM	6/6	5/9
	Dutly & Schinzel (1996) (30): WBS	15/15	-
	Total :	22/22=1	**20/33=0.61**
8p23.1	Girirajan *et al.* (2012) (1): DD/ASD/CM	2/5=0.40	2/10=0.20
9q34	Girirajan *et al.* (2012) (1): DD/ASD/CM	9/9=1	2/6=0.33
10q23	Girirajan *et al.* (2012) (1): DD/ASD/CM	5/13=0.38	0/3=0
15q11.2	Doornbos *et al.* (2009) (31): MR	2/9	NA
	de Kovel *et al.* (2010) (32): epilepsy	0/4	
	Kirov *et al.* (2012) (15): SCZ	2/5	
	Shen *et al.* (2010) (19): ASD	0/1	
	Levy *et al.* (2011) (21): ASD	1/6	
	Burnside *et al.* (2011) (33) & pers. comm. 13.6.2011: DD/CM	1/24	
	Malhotra *et al.* (2011) (10): SCZ/BD/controls	0/4	
	Girirajan *et al*. (2011) (27): DD/AU/Dyslexia	1/1	

Locus	Reference	Deletions	Duplications
	Rosenfeld *et al*. (2012) (2): DD/ASD/CM **Total:**	0/27 **7/81=0.09**	
15q13.3	Sharp *et al.* (2008) (34): MR van Bon *et al.* (2009) (35): MR de Kovel *et al.* (2010) (32): epilepsy Buysse *et al.* (2009) (7): MR Dibbens *et al.* (2009) (36): epilepsy Guilmatre *et al.* (2009) (13): MR Shen *et al.* (2010) (19): ASD Kirov *et al.* (2012) (15): SCZ Sanders *et al.* (2011) (22): ASD Malhotra *et al*. (2011) (10): SCZ/BD/controls Girirajan *et al.* (2011) (27): DD/AU/Dyslexia Griswold *et al.* (2012) (11): AU Girirajan *et al.* (2012) (1): DD/ASD/CM **Total :**	2/4 3/14 1/5 0/2 3/5 1/1 0/1 2/2 1/2 - 1/1 1/1 7/33 **22/71=0.31**	- 1/1 - - - 0/1 - - 1/1 0/1 - - 0/11 2/15=0.13
15q11-13 (AS/PWS)	Guilmatre *et al.* (2009) (13): ASD Glessner *et al.* (2009) (14): ASD Ingason *et al.* (2011) (37): SCZ Marshall *et al.* (2008) (38): ASD Sanders *et al.*/Levy *et al.* (2011) (21, 22): ASD Girirajan *et al.* (2012) (1): DD/ASD/CM Butler *et al.* (1986) (39): PWS Chan *et al*. (1993) (40): AS **Total:**	- - - - - 11/13 21/21PWS 47/47AS 79/81=0.98	1/1 2/8 1/1 2/2 1/1 10/21 **-** **-** **17/34=0.50**
15q24	Girirajan *et al.* (2012) (1): DD/ASD/CM Magoulas & El-Hattab (2012) (41): 15q24 syndrome **Total**:	5/5 18/18 23/23=1	0/1 - 0/1
15q24.2-q24.3	Girirajan *et al.* (2012) (1)	4/4	0/1
15q25	Girirajan *et al.* (2012) (1): DD/ASD/CM Girirajan *et al*. (2013) (12): ASD **Total** :	- 0/1 0/1	1/1 0/1 1/2=0.50
Rubinstein-Taybi	Girirajan *et al.* (2012) (1): DD/ASD/CM	1/1	-

Locus	Reference	Deletions	Duplications
	Hennekam *et al*. (1993) (42): Rubinstein-Taybi	(99%)	
16p13.1	Buysse *et al.* (2009) (7): MR	0/1	1/1
	Ullmann *et al.* (2007) (43): MR/AU	1/3	0/2
	Hannes *et al.* (2008) (44): MR	0/1	1/4
	Kirov *et al.* (2012) (15): SCZ	-	0/1
	Williams *et al.* (2010) (45): ADHD	-	1/2
	Nagamani *et al.* (2011) (46): various phenotypes	2/3	0/7
	Sanders *et al.* (2011) (22): ASD	1/2	2/6
	Kuang *et al*. (2011) (47): Aortic aneurism	**-**	1/2
	Malhotra *et al.* (2011) (10): controls	**-**	0/1
	Girirajan *et al*. (2011) (27): DD,AU,Dyslexia	0/2	0/2
	Girirajan *et al*. (2012) (1): DD/ASD/CM	-	3/40
	Rosenfeld *et al*. (2012) (2): DD/ASD/CM	5/23	-
	Totals:	**9/35=0.26**	**9/68=0.13**
16p11.2p12.1	Girirajan *et al*. (2012) (1): DD/ASD/CM	4/6=0.67	2/5=0.40
16p12.1	Girirajan *et al*. (2012) (1): DD/ASD/CM	1/25=0.04	1/7=0.14
16p11.2distal	Bochukova *et al*. (2010) (48): obesity	0/2del	-
	Bachmann-Gagescu *et al*. (2010) (49): DD, various phenotypes	5/13del	4/5dup
	Guha *et al*. (2013) (50): SCZ	0/2del	-
	Barge-Schaapveld *et al*. (2011) (51): DD	0/2 del	-
	Bijlsma *et al*. (2009) (52): MR/CM	0/1del	-
	Rosenfeld *et al*. (2012) (2): DD/ASD/CM	7/21del	1/8dup
	Totals :	**12/41=0.29**	5/13=0.38
16p11.2	Walsh *et al.* (2008) (53): SCZ	-	0/2
	Guilmatre *et al.* (2009) (13): SCZ/MR	2/3	1/3
	McCarthy *et al.* (2009) (54): SCZ	-	0/5
	Fernandez *et al.* (2010) (55): ASD	2/3	1/3
	Buysse *et al.* (2009) (7): MR	0/3	1/2
	Glessner *et al.* (2009) (14): ASD	5/5	1/8
	Grozeva *et al.* (2010) (56): BD	-	1/1
	Kirov *et al,* (2012) (15): SCZ	-	1/2
	Shen *et al.* (2010) (19): ASD	-	0/1
	Bremer *et al.* (2011) (20): ASD	-	0/1

Locus	Reference	Deletions	Duplications
	Sanders *et al.* (2011) (22): ASD	7/8	4/6
	Shinawi *et al.* (2010) (57): DD/CM	8/10	3/5
	Malhotra *et al*. (2011) (10): BD/SZ/controls	-	1/2
	Girirajan *et al*. (2011) (27): DD,ASD,Dyslexia	-	3/3
	Griswold *et al.* (2012) (11): AU	1/1	1/2
	Rosenfeld *et al.* (2012) (2): DD/ASD/CM	33/47	7/30
	Totals :	58/80=0.72	**25/76=0.33**
17p13.3(YWHAE)	Girirajan *et al.* (2012) (1): DD/ASD/CM	3/3	4/8=0.50
Smith Magenis/ Potocki Lupski Syndrome	Girirajan *et al.* (2012) (1): DD/ASD/CM	4/4	4/4
	Girirajan *et al.* (2013) (12): ASD	-	1/1
	Smith *et al*. (1999) (58): no specific numbers given	"100%"	-
	Totals:	100%	5/5=1
NF1	Girirajan *et al.* (2012) (1)	-	1/3
17q12	Moreno-De-Luca *et al.* (2010) (59): ASD/SCZ, others	7/8	-
	Rosenfeld *et al*. (2012) (2): DD/ASD/CM	5/9	2/9
	Girirajan *et al*. (2013) (12): ASD	1/2	**-**
	Totals:	**13/19=0.68**	2/9=0.22
17q21.31	Girirajan *et al.* (2012) (1): DD/ASD/CM	10/10=1	1/2
17q23	Girirajan *et al.* (2012) (1): DD/ASD/CM	1/1	1/1
19p13.12	Girirajan *et al.* (2012) (1): DD/ASD/CM	2/2	NA
22q11.21	Buysse *et al.* (2009) (7): MR	5/5	-
	De Kovel *et al.* (2010) (32): epilepsy	1/1	-
	Marshall *et al.* (2008) (38): ASD	1/1	-
	Xu *et al.* (2008) (60): SCZ	3/3	-
	Swillen *et al.* (1998) (61): VCFS/DiGeorge Syndrome	85/97	-
	Digilio *et al.* (1997) (62): MR/DD	26/33	-
	Smith and Robson (1999) (58): VCFS/DiGeorge Syndrome	33.5/36.5	-
	Ryan *et al.* (1997) (63): DiGeorge Syndrome	204/285	-
	Thompson and Davies (1998) (64): VCFS/DiGeorge Syndrome	37/41	-
	Driscoll *et al.* (1993) (65): VCFS/DiGeorge Syndrome	57/63	-
	Worthington *et al.* (1998) (66): CHD	13/15	-
	Sanders *et al.* (2011) (22): ASD	1/1	-
	Girirajan *et al.* (2012) (1): DD/ASD/CM	16/20	-

Locus	Reference	Deletions	Duplications
	Rosenfeld *et al*. (2012) (2): DD/ASD/CM **Totals:**	- **482.5/601.5 =0.80**	12/47 12/47=0.26
22q11.2 distal	Girirajan *et al*. (2012) (1): DD/ASD/CM	8/8=1	1/6=0.17
Phelan-McDermid	Girirajan *et al*. (2012) (1): DD/ASD/CM	17/18=0.94	0/2

ADHD, attention-deficit/hyperactivity disorder; AS, Angelman syndrome; ASD, autism spectrum disorder; AU, autism; BD, bipolar disorder; CHD, congenital heart disease; CM, congenital malformations; CNV, copy number variant; DD, developmental delay; MR, mental retardation; PWS, Prader–Willi syndrome; SCZ, schizophrenia; VCFS, velo-cardio-facial syndrome; WBS, Williams-Beuren syndrome.

Table S4. Summary of the frequencies and penetrance of CNVs in the different phenotypes, and their 95% confidence intervals (95% CI). The *p*-value refers to the difference in the frequencies between SCZ and the group of DD/ASD/CM. All significant ones are for frequencies that are higher in the DD/ASD/CM group.

Locus	Position	Frequency %, 95% CI				*p*-value SCZ vs. DD/ASD/CM	Penetrance %, 95% CI			Selection Coefficient
		Controls	SCZ	DD/ASD/CM	General Population		SCZ	DD/ASD/CM	Total	
1p36 del	chr1:0,00-10,07	0.000 0-0.021	0.000 0-0.028	0.239 0.192-0.298	0.0096 0.0076-0.032	5.9×10^{-7}	0 0-3.6	100 23-100	100 23-100	0.82
1q21.1 del	chr1:146,57-147,39	0.021 0.013-0.034	0.173 0.123-0.243	0.292 0.225-0.379	0.0331 0.023-0.05	ns	5.2 2.5-11	35 18-67	40 20-78	0.26
1q21.1 dup	chr1:146,57-147,39	0.037 0.025-0.055	0.129 0.084-0.197	0.205 0.162-0.26	0.0451 0.031-0.065	ns	2.9 1.3-6.3	18 10-33	21 11-39	0.23
NRXN1 del	chr2:50,14-51,26	0.020 0.011-0.037	0.176 0.125-0.247	0.181 0.104-0.316	0.0276 0.016-0.05	ns	6.4 2.5-8.3	26 16-80	33 18-88	0.23
2q23.1 del	chr2:148,72-149,29	0.000 0-0.021	0.007 0.0012-0.041	0.061 0.039-0.094	0.0025 0.0016-0.024	0.014	2.9 0-26	97 6.5-100	100 6.5-100	
2q37 del	chr2:239,71-242,47	0.000 0-0.021	0.000 0-0.029	0.052 0.032-0.083	0.0021 0.0013-0.024	0.0054	0 0-23	100 5.5-100	100 5.5-100	
2q37 dup	chr2:239,71-242,47	0.000 0-0.021	0.000 0-0.029	0.006 0.0016-0.022	0.0002 0-0.021	ns	0 0-100	100 0-100	100 0-100	

Locus	Position	Frequency %, 95% CI				*p*-value SCZ vs. DD/ASD/CM	Penetrance %, 95% CI			Selection Coefficient
		Controls	SCZ	DD/ASD/CM	General Population		SCZ	DD/ASD/CM	Total	
3q29 del	chr3:195,73-197,34	0.001 0-0.0055	0.082 0.049-0.138	0.061 0.039-0.094	0.0046 0.002-0.01	ns	18 4.7-67	53 15-100	71 20-100	0.83
3q29 dup	chr3:195,73-197,34	0.000 0-0.021	0.000 0-0.029	0.055 0.035-0.087	0.0022 0.0014-0.024	0.003	0 0-21	100 5.9-100	100 5.9-100	0.16
Wolf-Hirschhorn del	chr4:1,53-2,03	0.000 0-0.021	0.000 0-0.029	0.052 0.032-0.083	0.0021 0.0013-0.024	0.0054	0 0-23	100 5.4-100	100 5.4-100	
Wolf-Hirschhorn dup	chr4:1,53-2,03	0.000 0-0.021	0.000 0-0.029	0.012 0.0046-0.031	0.0005 0.0002-0.022	ns	0 0-100	100 1-100	100 1-100	
Sotos syndrome del	chr5:175,72-177,06	0.000 0-0.021	0.000 0-0.029	0.043 0.026-0.072	0.0017 0.001-0.023	0.015	0 0-28	100 4.5-100	100 4.5-100	
Sotos syndrome dup	chr5:175,72-177,06	0.000 0-0.021	0.007 0.0012-0.041	0.012 0.0026-0.031	0.0006 0.0001-0.022	ns	13 0-100	87 0.5-100	100 0.5-100	
6p25 del	chr6:0,16-6,06	0.000 0-0.021	0.000 0-0.029	0.071 0.047-0.106	0.0028 0.0019-0.024	0.0007	0 0-15	100 7.7-100	100 7.7-100	0.08
6p25 dup	chr6:0,16-6,06	0.000 0-0.021	0.000 0-0.029	0.037 0.021-0.065	0.0015 0.0008-0.023	0.0024	0 0-35	100 3.7-100	100 3.7-100	0
6q16 (SIM1) del	chr6:100,84-100,91	0.000 0-0.021	0.000 0-0.029	0.004 0.0007-0.024	0.0002 0.00003-0.021	ns	0 0-100	100 0-100	100 0-100	
6q16 (SIM1) dup	chr6:100,84-100,91	0.006 0.0009-0.032	0.000 0-0.029	0.004 0.0007-0.024	0.0055 0.0008-0.032	ns	0 0-33	3.1 0-100	3.1 0-100	
WBS del	chr7:72,74-74,14	0.000 0-0.021	0.000 0-0.029	0.255 0.206-0.316	0.0102	4.6×10^{-13}	0 0-3.5	100 25-100	100 25-100	1
WBS dup	chr7:72,74-74,14	0.006 0.0016-0.021	0.066 0.039-0.11	0.120 0.088-0.164	0.011 0.0054-0.028	ns	6.0 1.4-20	44 13-100	50 14-100	0.61
8p23.1 del	chr8:8,09-11,89	0.000 0-0.021	0.007 0.0013-0.042	0.055 0.035-0.087	0.0023 0.0014-0.024	0.02	3.3 0-30	97 5.9-100	100 5.9-100	0.4
8p23.1 dup	chr8:8,09-11,89	0.000 0-0.021	0.000 0-0.029	0.074 0.05-0.11	0.0029 0.002-0.025	0.0004	0 0-14	100 8.1-100	100 8.1-100	0.2
9q34 del	chr9:137,81-141,08	0.000 0-0.021	0.000 0-0.029	0.055 0.035-0.087	0.0022 0.0014-0.024	0.003	0 0-21	100 5.9-100	100 5.9-100	1

Locus	Position	Frequency %, 95% CI				*p*-value SCZ vs. DD/ASD/ CM	Penetrance %, 95% CI			Selection Coefficient
		Controls	SCZ	DD/ASD /CM	General Population		SCZ	DD/ASD /CM	Total	
9q34 dup	chr9:137,81-141,08	0.000 0-0.021	0.000 0-0.029	0.025 0.013-0.049	0.0010 0.0005-0.022	ns	0 0-56	100 2.3-100	100 2.3-100	0.33
10q23 del	chr10:81,96-88,80	0.000 0-0.021	0.000 0-0.029	0.086 0.06-0.124	0.0034 0.0024-0.025	0.000089	0 0-12	100 9.5-100	100 9.5-100	0.38
10q23 dup	chr10:81,96-88,80	0.000 0-0.021	0.015 0.0041-0.054	0.015 0.0063-0.035	0.0008 0.0003-0.022	ns	19 0-100	81 1.1-100	100 1.1-100	
15q11.2 del	chr15:22,80-23,09	0.277 0.243-0.315	0.594 0.496-0.712	0.808 0.705-0.926	0.3019 0.264-0.343	0.0077	2.0 1.4-2.7	11 8.2-14	13 9.6-17	0.09
Prader-Willi/Angelman del	chr15:24,82-28,43	0.000 0-0.021	0.000 0-0.029	0.184 0.143-0.237	0.0074 0.0057-0.003	1.5×10^{-10}	0 0-5	100 19-100	100 19-100	0.98
Prader-Willi/Angelman dup	chr15:24,82-28,43	0.0083 0.0035-0.019	0.079 0.045-0.138	0.252 0.203-0.313	0.0187 0.012-0.032	0.00003	4.2 1.4-12	54 25-100	58 26-100	0.5
15q13.3 del	chr15:31,13-32,48	0.019 0.012-0.031	0.140 0.096-0.205	0.261 0.211-0.323	0.0296 0.021-0.044	0.004	4.7 2.2-9.9	35 19-62	40 21-72	0.31
15q13.3 dup	chr15:31,13-32,48	0.039 0.019-0.081	0.074 0.04-0.136	0.083 0.057-0.12	0.0413 0.021-0.083	ns	1.8 0.5-6.6	8.0 2.7-23	9.8 3.2-30	0.13
15q13.3 smaller (CHRNA7) del	chr15:32,01-32,45	0.000 0-0.021	0.015 0.004-0.054	0.030 0.015-0.062	0.0013 0.0006-0.023	ns	11 0.2-84	89 2.6-100	100 2.8-100	
15q13.3 smaller (CHRNA7) dup	chr15:32,01-32,45	0.733 0.618-0.869	0.616 0.497-0.763	0.556 0.468-0.66	0.7247 0.61-0.86	ns	0.9 0.6-1.2	3.1 2.2-4.3	4.0 2.8-5.5	
15q24 del	chr15:72,91-74,41	0.000 0-0.021	0.000 0-0.029	0.025 0.013-0.049	0.0010 0.0005-0.022	ns	0 0-56	100 2.3-100	100 2.3-100	1
15q24 dup	chr15:72,91-74,41	0.000 0-0.021	0.000 0-0.029	0.012 0.0046-0.031	0.0005 0.0002-0.022	ns	0 0-100	100 0.9-100	100 0.9-100	
15q24.2q24.5 del	chr15:75,97-78,20	0.000 0-0.021	0.000 0-0.029	0.015 0.0063-0.035	0.0006 0.00025-0.022	ns	0 0-100	100 1.2-100	100 1.2-100	
15q24.2q24.5 dup	chr15:75,97-78,20	0.000 0-0.021	0.000 0-0.029	0.018 0.0063-0.035	0.0007 0.0002-0.022	ns	0 0-100	100 1.2-100	100 1.2-100	
15q25 del	chr15:83,18-84,74	0.000 0-0.021	0.000 0-0.029	0.009 0.0025-0.032	0.0003 0.0001-0.022	ns	0 0-100	100 0.5-100	100 0.5-100	

Locus	Position	Frequency %, 95% CI				*p*-value SCZ vs. DD/ASD/CM	Penetrance %, 95% CI			Selection Coefficient
		Controls	SCZ	DD/ASD/CM	General Population		SCZ	DD/ASD/CM	Total	
15q25 dup	chr15:83,18-84,74	0.000 0-0.021	0.000 0-0.029	0.017 0.0066-0.044	0.0007 0.00026-0.022	ns	0 0-100	100 1.2-100	100 1.2-100	
16p13.11 del	chr16:15,51-16,30	0.039 0.019-0.081	0.074 0.04-0.136	0.150 0.114-0.198	0.044 0.023-0.086	0.045	1.7 0.5-5.9	14 5.3-34	15 5.8-40	0.26
16p13.11 dup	chr16:15,51-16,30	0.134 0.109-0.164	0.308 0.224-0.424	0.301 0.247-0.367	0.1426 0.116-0.175	ns	2.2 1.3-3.7	8.4 5.7-13	10.6 7-17	0.13
16p11.2p12.1 del	chr16:21,53-29,10	0.000 0-0.021	0.000 0-0.029	0.061 0.039-0.094	0.0025 0.0016-0.024	0.002	0 0-19	100 6.5-100	100 6.5-100	0.67
16p11.2p12.1 dup	chr16:21,53-29,10	0.000 0-0.021	0.000 0-0.029	0.043 0.026-0.072	0.0017 0.001-0.023	0.015	0 0-28	100 4.4-100	100 4.4-100	0.4
16p12.1 del	chr16:21,94-22,46	0.05 0.026-0.095	0.178 0.120-0.265	0.187 0.146-0.24	0.0571 0.032-0.1	ns	3.1 1.2-8.3	13 5.7-30	16 6.9-38	0.04
16p12.1 dup	chr16:21,94-22,46	0.05 0.026-0.095	0.037 0.016-0.087	0.049 0.03-0.07	0.0502 0.027-0.094	ns	0.7 0.2-3.3	3.9 1.3-11	4.8 1.5-14	0.14
16p11.2 distal del	chr16:28,82-29,05	0.018 0.0076-0.043	0.063 0.037-0.108	0.138 0.103-0.184	0.0237 0.012-0.049	0.01	2.6 0.8-9.2	23 8.4-63	26 9.2-72	0.29
16p11.2 distal dup	chr16:28,82-29,05	0.056 0.03-0.103	0.037 0.016-0.087	0.075 0.051-0.111	0.0565 0.031-0.103	ns	0.7 0.2-2.8	5.3 2-14	6.0 2.2-17	0.38
16p11.2 del	chr16:29,64-30,20	0.041 0.028-0.06	0.030 0.013-0.07	0.439 0.373-0.516	0.0570 0.042-0.078	3.9×10^{-20}	0.5 0.2-1.7	31 19-50	31 19-52	0.72
16p11.2 dup	chr16:29,64-30,20	0.030 0.019-0.047	0.346 0.268-0.447	0.280 0.229-0.343	0.0433 0.032-0.063	ns	8.0 4.3-14	26 18-43	34 22-57	0.33
Rubinstein-Taybi del	chr16:3,78-3,93	0.006 0.0001-0.032	0.000 0-0.029	0.031 0.017-0.057	0.0065 0.0008-0.033	0.04	0 0-37	19 2-100	19 2-100	0.99
17p13.3 (YWHAE) del	chr17:1,25-1,30	0.006 0.0001-0.032	0.000 0-0.029	0.021 0.01-0.044	0.0062 0.0005-0.032	ns	0 0-59	14 1.2-100	14 1.2-100	
17p13.3 (YWHAE) dup	chr17:1,25-1,30	0.017 0.0059-0.05	0.022 0.0074-0.065	0.040 0.023-0.068	0.0178 0.0066-0.051	ns	1.3 0.1-9.8	9.0 1.8-41	10.3 1.9-51	0.5
17p13.3(PAFAH1B1) del	chr17:2,49-2,59	0.000 0-0.021	0.000 0-0.029	0.025 0.013-0.049	0.0010 0.0005-0.022	ns	0 0-56	100 2.3-100	100 2.3-100	

Locus	Position	Frequency %, 95% CI				*p*-value SCZ vs. DD/ASD/ CM	Penetrance %, 95% CI			Selection Coefficient
		Controls	SCZ	DD/ASD /CM	General Population		SCZ	DD/ASD /CM	Total	
17p13.3(PAFAH1B1) dup	chr17:2,49-2,59	0.006 0.0001-0.032	0.000 0-0.029	0.028 0.015-0.053	0.0064 0.0007-0.032	ns	0 0-42	17 1.8-100	17 1.8-100	
Smith-Magenis del	chr17:16,82-18,28	0.000 0-0.021	0.000 0-0.029	0.095 0.067-0.135	0.0038 0.0027-0.026	0.000032	0 0-11	100 10-100	100 10-100	1
Potocki-Lupski (dup)	chr17:16,82-18,28	0.000 0-0.021	0.007 0.0013-0.042	0.077 0.052-0.114	0.0031 0.0021-0.025	0.0021	2.4 0.1-20	98 8-100	100 8-100	1
NF1 del	chr17:29,10-30,28	0.006 0.0001-0.032	0.000 0-0.029	0.080 0.055-0.117	0.0085 0.0023-0.036	0.00027	0 0-13	38 6-100	38 6-100	
NF1 dup	chr17:29,10-30,28	0.000 0-0.021	0.007 0.0013-0.042	0.107 0.077-0.149	0.0044 0.003-0.027	0.00013	1.7 0-14	98 12-100	100 12-100	
17q12 del	chr17:34,81-36,20	0.005 0.0021-0.014	0.036 0.015-0.084	0.087 0.061-0.125	0.009 0.0046-0.019	ns	4.0 0.8-18	39 13-100	43 14-100	0.68
17q12 dup	chr17:34,81-36,20	0.022 0.0085-0.057	0.045 0.021-0.098	0.111 0.081-0.153	0.0262 0.012-0.061	0.029	1.7 0.3-8.5	17 5.3-53	19 5.6-61	0.22
17q21.31 del	chr17:43,70-44,18	0.000 0-0.021	0.000 0-0.029	0.129 0.096-0.174	0.0052 0.0038-0.027	10^{-6}	0 0-7.6	100 14-100	100 14-100	1
17q21.31 dup	chr17:43,70-44,18	0.000 0-0.021	0.007 0.0013-0.042	0.015 0.0064-0.035	0.0007 0.0003-0.022	ns	10.8 0.1-100	89 1.2-100	100 1.3-100	
17q23 del	chr17:58,25-60,29	0.000 0-0.021	0.000 0-0.029	0.018 0.0082-0.039	0.0007 0.0003-0.022	ns	0 0-88	100 1.5-100	100 1.5-100	
17q23 dup	chr17:58,25-60,29	0.000 0-0.021	0.000 0-0.029	0.003 0.0005-0.017	0.0001 0.00002-0.021	ns	0 0-100	100 0-100	100 0-100	
19p13.12 del	chr19:13,08-16,70	0.000 0-0.021	0.000 0-0.029	0.04 0.023-0.068	0.0016 0.0009-0.023	0.014	0 0-32	100 4-100	100 4-100	
DiGeorge/VCFS del	chr22:19,02-20,26	0.000 0-0.005	0.293 0.226-0.38	0.537 0.463-0.662	0.0244 0.021-0.035	0.00005	12 6.5-18	88 53-100	100 60-100	0.8
22q11.21 dup	chr22:19,02-20,26	0.075 0.051-0.111	0.019 0.0064-0.056	0.280 0.237-0.331	0.0824 0.058-0.119	4.5×10^{-13}	0 0-1	14 8-23	14 8-24	0.26
22q11.2distal del	chr22:21,91-23,65	0.000 0-0.021	0.000 0-0.029	0.111 0.076-0.163	0.0044 0.003-0.027	0.000012	0 0-9.5	100 11-100	100 11-100	1

Locus	Position	Frequency %, 95% CI				*p*-value SCZ vs. DD/ASD/CM	Penetrance %, 95% CI			Selection Coefficient
		Controls	SCZ	DD/ASD /CM	General Population		SCZ	DD/ASD /CM	Total	
22q11.2distal dup	chr22:21,91-23,65	0.017 0.0058-0.05	0.007 0.0012-0.041	0.077 0.049-0.123	0.0191 0.0075-0.053	0.0032	0 0-5.5	16 3.7-66	17 3.7-72	0.17
Phelan-McDermid del	chr22:43,00-51,16	0.000 0-0.021	0.000 0-0.029	0.181 0.14-0.233	0.0072 0.0056-0.03	2.4×10^{-9}	0 0-5.2	100 19-100	100 19-100	0.94
22q13 dup	chr22:43,00-51,16	0.000 0-0.021	0.000 0-0.029	0.009 0.003-0.027	0.0004 0.0001-0.021	ns	0 0-100	100 0.6-100	100 0.6-100	

See Table S2 for abbreviations.

Table S5. Comparison of penetrance estimates from this study with those from the main previous publications. "Vassos" refers to Vassos *et al.* (67); "Rosenfeld" refers to the study by Rosenfeld *et al.* (2).

Locus	Current Study Penetrance SCZ	Vassos Penetrance SCZ	Current Study Penetrance DD/CM/ASD	Rosenfeld Penetrance DD/ASD/CM
1q21.1 del	5.2 (2.5-11)	6.1 (3-12)	35 (18-67)	37 (23-55)
1q21.1 dup	2.9 (1.3-6.3)		18 (10-33)	29 (17-47)
NRXN1 del	6.4 (2.5-8.3)	2.0 (1-4)	26 (16-80)	
15q11.2 del	2.0 (1.4-2.7)	2.0 (1-3)	10.7 (8.2-14)	10 (8.4-13)
15q13.3 del	4.7 (2.2-9.9)	7.4 (3-16)	35 (19-62)	
16p13.11 del	1.7 (0.5-5.9)		14 (5.3-34)	13 (7.9-21)
16p13.11 dup	2.2 (1.3-3.7)	2.4 (1-4)	8.4 (5.7-13)	
16p12.1 del	3.1 (1.2-8.3)		13 (5.7-30)	12 (7.9-19)
16p11.2 distal del	2.6 (0.8-9.2)		23 (8.4-63)	62 (27-94)
16p11.2 distal dup	0.7 (0.2-2.8)		5.3 (2-14)	11 (6.3-20)
16p11.2 del	0.5 (0.2-1.7)		31 (19-50)	47 (32-64)
16p11.2 dup	8.0 (4.3-14)	6.9 (3-14)	26 (18-43)	27 (17-41)
17q12 del	4.0 (0.8-18)		39 (13-100)	34 (14-70)
17q12 dup	1.7 (0.3-8.5)		17 (5.3-53)	21 (11-40)
DiGeorge/VCFS del	12 (6.5-18)	55 (18-97)	88 (53-100)	
22q11.21 dup	0.2 (0-1)		14 (8-23)	22 (15-32)

See Table S2 for abbreviations.

Table S6. Presence of a "second hit" CNV in carriers of a selected list of CNV loci that have been implicated in SCZ. A "second hit" is defined as a CNV of >500 kb in size (deletion or duplication) that is found in <0.1% of the control populations used in this study, or a CNV from the list in Table S2, even if smaller than 500 kb (following the definition used by Girirajan *et al.* (1)). The analysis of second hits was performed on the 13,465 cases and 17,873 controls (listed under D in Table S2): 6882 cases / 11,255 controls from the "Current sample" + 3391 cases / 3181 controls from the ISC study + 3192 cases / 3437 controls from the MGS study.

Locus	% Double Hits (N_double hits/N_carriers, SCZ)	% Double Hits (N_double hits/N_carriers, Controls)	% Double Hits in DD/ASD/CM from ref (1)
1q21.1 del	16.7% (4/24)	0% (0/6)	8% (8/100)
1q21.1 dup	18.8% (3/16)	12.5% (1/8)	4.9% (4/81)
3q29 del	0% (0/10)	0% (0/0)	20.0% (4/20)
WBS dup	28% (2/7)	0% (0/2)	5.1% (2/39)
15q11.2 del	11.9% (10/84)	6.8% (5/73)	16.3% (27/166)
Angelman /Prader-Willi dup	16.7% (2/12)	0% (0/0)	6.1% (5/82)
15q13.3 del	5.9% (1/17)	0% (0/4)	8.2% (7/85)
16p13.11 dup	6.7% (3/45)	10% (4/40)	8.2% (8/98)
16p11.2 distal del	0% (0/5)	0% (0/4)	12.9% (4/31)
16p11.2 dup	7.3% (3/41)	0% (0/4)	14.5% (12/83)
17q12 del	50% (1/2)	0% (0/0)	11.5% (3/26)
22q11.2 del	4.2% (2/48)	0% (0/0)	4.6% (8/175)
Overall %:	10.0% (31/311)	7.1% (10/141)	9.3% (92/986)

See Table S2 for abbreviations.

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