Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods. DNA Extraction and CNV Calling

DNA extraction For all individuals within the iPSYCH case-cohort, DNA was extracted and whole-genome amplified from available neonatal blood spots retrieved from the Danish Neonatal Screening Biobank (DNSB) [1], and genotyped with the Illumina Infinium PsychArray BeadChip Kit (Illumina, San Diego, CA, USA), as previously described [2]. Samples with blood spots available to analysis included 52,867 cases and 28,650 cohort individuals. Single nucleotide polymorphism (SNP) variant calling and quality control were performed using Illumina's GenTrain software tool. The extraction of B-allele frequency as well as intensity for each probe was performed using Illumina GenomeStudio. Samples with genotyping call rate lower than 97% or genotype-estimated sex discordance with the Danish Civil Registration System were excluded. Individuals with sex chromosome aneuploidy were also excluded. After QC, the sample included 49,250 cases and 25,704 cohort samples (see eTable 1); the rate of samples lost to genotyping and QC was around 14% and did not differ between cases and controls (Fisher's exact test; p=0.59).

CNV calling The current study considers deletions and duplications at the following six loci (1q21.1, 15q11.2, 15q13.3, 16p11.2, 17p12 and 17q12; see eTable 1 for hg19 coordinates and number of probes at each locus) as well as at the 22q11.2 locus previously examined in the case-cohort [3]. These 7 loci represent a coherent set for comparative analysis because CNVs at these loci have been previously suggested to be involved in psychiatric disorders [4-9] and they are located within chromosomal regions suitable for reliable CNV calling. Deletions and duplications at these loci were identified using the gold-standard CNV calling algorithm, PennCNV [10], supplemented with iPSYCH CNV (an in-house developed algorithm to optimize CNV identification from WGA-DNA) [11], and subsequent careful, visual inspection of each call including 15 or more probes with at least 10 probes overlapping the respective locus, as previously described in detail [3].

The validation of CNV calls was based on three types of evidence: *First*, for each locus, we divided the total iPSYCH case-cohort into quartiles based on the standard deviation of the log R ratio (LRR-SD) and compared the frequency of deletion and duplication calls across the quartiles. Increased LRR-SD reflects poorer sample quality, and the reduced signal-to-noise ratio increases the risk of the CNV algorithms making spurious calls. Consistently, we observe more calls in the 4th LRR-SD quartile than in the remaining 3 quartiles (eFigure1). To reduce the number of spurious calls, we progressively excluded noisy samples based on LRR-SD until the difference in CNV call frequency across quartiles was equal to or smaller than five percent. As experimental noise varies across genomic regions, the LRR-SD threshold value differs between loci and consequently also the

number of samples evaluated at each locus (eTable 1). *Second*, all CNV calls detected by at least one of the two CNV calling algorithms were plotted for visual inspection of the distribution of the B-Allele Frequency (BAF) and LRR, and independently evaluated by several researchers to obtain consensus calls. *Third*, samples with uncertain consensus calls (n=368) plus a random set of visually validated true and false calls (n=164) were re-genotyped using unamplified, genomic DNA on the Infinium Omni2.5-8 version 1.3 BeadChip (Illumina, San Diego, CA, USA) for clarification (uncertain calls) and verification of the visual evaluations. The fraction of samples labelled as 'uncertain consensus calls' and therefore subjected to re-genotyping was 77% cases and 23% cohort. The higher rate among cases is expected as CNVs confer risk of disease. Importantly the case-cohort ratio of 'uncertain consensus calls' was not significantly different from that of confirmed CNV calls ($p=0.23$); also the confirmation rate (75%) did not differ between cases and cohort ($p=0.26$).

eTable 1. Per locus details for CNV calling for iPSYCH case-cohort. **Out of the initial sample of 86,189 individuals (57,377 cases, 30,000 cohort), a total of 73,923 individuals passed genotyping QC (49,250 cases, 25,704 cohort)**

Locus	Genomic position	# probes	Length (MB)	LRR-SD treshold	Inspected deletions	Inspected duplications	Confirmed deletions	Confirmed duplications	Post per locusQC sample size
1q21.1	chr1:146330584-147825662	288	1,5	0.36	65	99	46	96	68196
15q11.2	chr15:22770994-23164467	136	0,39	0.34	432	387	348	333	64428
15q13.3	chr15:30916171-32637706	300	1,7	0.34	40	72	37	70	69873
16p11.2	chr16:29595483-30156963	241	0,56	0.33	152	156	37	108	54364
17p12	chr17:14005459-15510011	334	1,5	0.47	33	44	31	17	73146
17q12	chr17:34815551-36249430	370	1,4	0.35	37	37	21	36	63520

eTable 2. Case-cohort subgroups: Frequencies of study subjects and CNVs frequencies						
Locus	Case-cohort subgroup	Samples (n)[§]	Deletions (%)	Duplications (%)	Deletions (n)	Duplications (n)
AnyCNV^	Case-Cohort	53859	0.75	1.03	404	553
	Cohort	**19014**	**0.54**	**0.82**	**103**	**155**
	Cases	35597	0.86	1.13	305	403
	Overlap*	752	-	-	-	-
	SCZ	1671	0.78	1.20	13	20
	BPD	919	0.54	0.54	5	5
	MDD	14870	0.75	0.93	112	138
	ASD	10956	1.03	1.13	113	124
	ADHD	12633	0.83	1.35	105	170
	ID	3338	1.47	1.77	49	59
	Epilepsy	1842	1.52	0.92	28	17
1q21.1	Case-Cohort^	68196	0.067	0.14	46	96
	Cohort	**23780**	**0.021**	**0.097**	**5**	**23**
	Cases	45361	0.090	0.17	41	75
	Overlap*	945	-	-	-	-
	SCZ	2344	<0.21	<0.21	<5	<5
	BPD	1272	<0.39	<0.39	<5	<5
	MDD	18812	0.074	0.096	14	18
	ASD	13196	0.11	0.28	15	37
	ADHD	15256	0.11	0.18	17	28
	ID	3985	0.25	0.20	10	8
	Epilepsy	2261	<0.22	<0.22	<5	<5
15q11.2	Case-Cohort^	64428	0.54	0.52	348	333
	Cohort	**22506**	**0.44**	**0.49**	**99**	**111**
	Cases	42816	0.59	0.53	253	227
	Overlap*	894	-	-	-	-
	SCZ	2190	0.50	0.46	11	10
	BPD	1196	<0.42	0.42	<5	5
	MDD	17679	0.55	0.52	97	91
	ASD	12520	0.66	0.46	82	58
	ADHD	14429	0.58	0.58	84	84
	ID	3785	0.66	0.61	25	23
	Epilepsy	2144	0.98	0.42	21	9
15q13.3	Case-Cohort^	69873	0.053	0.10	37	70
	Cohort	**24326**	**0.021**	**0.062**	**5**	**15**
	Cases	46519	0.069	0.12	32	56
	Overlap*	972	-	-	-	-

	SCZ	2439	<0.21	<0.21	<5	<5
	BPD	1320	0	<0.38	0	<5
	MDD	19342	0.078	0.12	15	23
	ASD	13488	0.074	0.12	10	16
	ADHD	15615	0.070	0.13	11	20
	ID	4072	0.27	0.20	11	8
	Epilepsy	2309	0.22	<0.22	5	<5
16p11.2	Case-Cohort^	54364	0.068	0.20	37	108
	Cohort	**19169**	**0.052**	**0.11**	**10**	**21**
	Cases	35955	0.078	0.25	28	88
	Overlap*	760	-	-	-	-
	SCZ	1704	0	0.35	0	6
	BPD	925	0	0	0	0
	MDD	14071	<0.036	0.18	<5	25
	ASD	11022	0.15	0.29	17	32
	ADHD	12650	0.063	0.36	8	46
	ID	3316	<0.15	0.57	<5	19
	Epilepsy	1805	0.28	0.33	<5	6
17p12	Case-Cohort^	73146	0.042	0.023	31	17
	Cohort	**25431**	**0.051**	**0.024**	**13**	**6**
	Cases	48738	0.037	0.023	18	11
	Overlap*	1023	-	-	-	-
	SCZ	2590	<0.19	<0.19	<5	<5
	BPD	1384	<0.36	0	<5	0
	MD	20186	0.054	0.025	11	5
	ASD	14145	<0.035	<0.035	<5	<5
	ADHD	16427	<0.030	<0.030	<5	<5
	ID	4257	<0.12	<0.12	<5	<5
	Epilepsy	2405	0	<0.21	0	<5
17q12	Case-Cohort^	63520	0.033	0.057	21	36
	Cohort	**22185**	**0.023**	**0.023**	**5**	**5**
	Cases	42214	0.038	0.073	16	31
	Overlap*	879	-	-	-	-
	SCZ	2147	<0.23	<0.23	<5	<5
	BPD	1160	0	0	0	0
	MDD	17177	<0.029	0.047	<5	8
	ASD	12478	0.072	0.056	9	7
	ADHD	14403	0.049	0.12	7	17
	ID	3780	0.16	<0.13	6	<5
	Epilepsy	2123	0	<0.24	0	<5

§ Number of study subjects across CNV loci differs as locus-specific signal-to-noise ratio impacts on sample QC.

^ The number of CNVs observed in the case-cohort based on locus-specific QC criteria (i.e. 520 deletions and 660 duplications) is higher than the number of CNVs observed based on QC criteria shared across loci (reported as 'Any CNV': 404 deletions and 533 duplications). To highlight the impact of QC criteria, the rows showing observations in the Cohort are shown in bold.

* The Case-Cohort design by necessity results in an overlap between the Cohort and the Case group; i.e. #Case-cohort = #Cohort + #Cases - #Overlap For the entire Cohort and the Cases this overlap is 1,031 individuals, whereas the overlap differs between the analyses of each CNV locus as explained above^.

eTable 3. Frequencies of CNVs observed in the cohort by gender and mean age of carriers			
CNV	Female	Male	Mean age (s.d.)
1q21.1 del	<5	<5	17 (5)
1q21.1 dup	12	11	16 (6)
15q11.2 del	47	52	19 (7)
15q11.2 dup	63	48	18 (6)
15q13.3 del	<5	<5	20 (6)
15q13.3 dup	10	5	20 (7)
16p11.2 del	<5	7	14 (4)
16p11.2 dup	12	9	20 (6)
17p12 del	7	6	21 (8)
17p12 dup	5	<5	24 (5)
17q12 del	<5	<5	15 (7)
17q12 dup	<5	<5	20 (9)

eTable 4. Risk of neuropsychiatric and developmental disorders in CNV carriers

		Deletions					Duplications				
Locus	Diagnosis	HR	lower CI	upper CI	P-value	N	HR	lower CI	upper CI	P-value	N
1q21.1	SCZ	3.3	0.3	32.3	0.30	<5	1.5	0.3	7.6	0.61	<5
	BPD	9.1	0.9	89.8	0.060	<5	1.7	0.2	14.2	0.61	<5
	MDD	5.8	1.5	21.1	0.010	14	1.7	0.8	3.7	0.20	18
	ASD	5.1	1.6	15.8	0.0054	15	3.5	1.9	6.4	3.1×10^{-5}	37
	ADHD	5.4	1.8	16.6	0.0032	17	2.4	1.3	4.7	0.0064	28
	ID	-	-	-	-	10	7.0	0.9	52.6	0.058	8
	epilepsy	-	-	-	-	<5	-	-	-	-	<5
15q11.2	SCZ	1.0	0.5	2.0	0.89	11	1.2	0.6	2.5	0.58	10
	BPD	0.7	0.3	2.0	0.53	<5	1.1	0.4	2.7	0.91	5
	MDD	1.2	0.9	1.8	0.25	97	1.2	0.8	1.7	0.33	91
	ASD	1.4	1.0	2.0	0.029	82	1.0	0.7	1.5	0.76	58
	ADHD	1.2	0.9	1.7	0.18	84	1.3	1.0	1.8	0.062	84
	ID	1.3	0.2	9.4	0.79	25	-	-	-	-	23
	Epilepsy	1.4	0.4	5.7	0.61	21	1.3	3.2	5.2	0.71	9
15q13.3	SCZ	8.2	1.7	39.7	0.0092	<5	2.8	0.7	10.2	0.13	<5
	BPD	-	-	-	-	0	2.7	0.5	14.0	0.23	<5
	MDD	3.2	0.8	13.3	0.10	15	2.5	0.9	6.5	0.061	23
	ASD	3.6	1.1	12.1	0.040	10	2.5	1.1	5.7	0.029	16
	ADHD	3.4	1.1	11.0	0.041	11	2.6	1.1	5.8	0.029	20
	ID	-	-	-	-	11	-	-	-	-	8
	Epilepsy	-	-	-	-	5	-	-	-	-	<5
16p11.2	SCZ	-	-	-	-	0	2.7	1.0	7.4	0.056	6
	BPD	-	-	-	-	0	-	-	-	-	0
	MDD	1.7	0.4	6.7	0.46	<5	1.3	0.6	2.7	0.54	25
	ASD	2.6	1.2	6.0	0.021	17	2.7	1.4	4.8	0.0015	32
	ADHD	1.2	0.4	3.2	0.77	8	3.2	1.8	5.6	9.3×10^{-5}	46
	ID	-	-	-	-	<5	-	-	-	-	19
	Epilepsy	10.6	1.3	85.6	0.026	<5	6.6	1.7	25.6	0.0062	6
17p12	SCZ	0.6	0.1	4.6	0.59	<5	3.3	0.8	14.3	0.11	<5
	BPD	0.8	0.1	6.5	0.82	<5	-	-	-	-	0
	MDD	0.6	0.2	1.6	0.33	11	0.5	0.1	1.6	0.22	5
	ASD	0.6	0.2	1.9	0.39	<5	1.2	0.3	5.1	0.80	<5
	ADHD	0.4	0.1	1.3	0.11	<5	0.9	0.2	3.5	0.83	<5

	ID	-	-	-	-	<5	-	-	-	-	<5
	Epilepsy	-	-	-		0	10.2	1.5	71.4	0.018	<5
17q12	SCZ	4.2	0.3	65	0.30	<5	5.0	0.9	26.6	0.060	<5
	BPD	-	-	-	-	0	-	-	-	-	0
	MDD	0.3	0.0	5.0	0.43	<5	1.2	0.3	5.3	0.78	8
	ASD	6.8	2.0	22.9	0.0020	9	2.8	0.8	10.0	0.11	7
	ADHD	4.4	1.2	15.9	0.023	7	5.4	1.8	15.8	0.0023	17
	ID	-	-	-	-	6	-	-	-	-	<5
	Epilepsy	-	-	-	-	0	-	-	-	-	<5

eTable 5. CNV impact on male and female fertility rate.							
Locus	CNV	Females			Males		
		RR*	Lower CI	Upper CI	RR	Lower CI	Upper CI
1q21.1	Deletion	0.99	0.56	1.75	-	-	-
1q21.1	Duplication	0.98	0.57	1.69	0.26	0.07	1.06
15q11.2	Deletion	0.83	0.65	1.06	1.13	0.83	1.53
15q11.2	**Duplication**	0.95	0.75	1.20	**0.62**	**0.38**	**0.99**
15q13.3	Deletion	0.75	0.36	1.58	1.73	0.72	4.16
15q13.3	Duplication	1.01	0.67	1.78	1.24	0.69	2.24
16p11.2	Deletion	0.15	0.02	1.04	-	-	-
16p11.2	Duplication	0.69	0.42	1.14	1.25	0.63	2.51
17p12	Deletion	0.97	0.56	1.66	2.33	0.75	7.23
17p12	Duplication	1.05	0.50	2.20	-	-	-
17q12	Deletion	-	-	-	-	-	-
17q12	Duplication	0.75	0.28	1.98	0.78	0.29	2.07

* Risk ratio; relative change in number of offspring derived from a Poisson regression model with age and mental disorders as covariates. Significant findings are shown in bold.

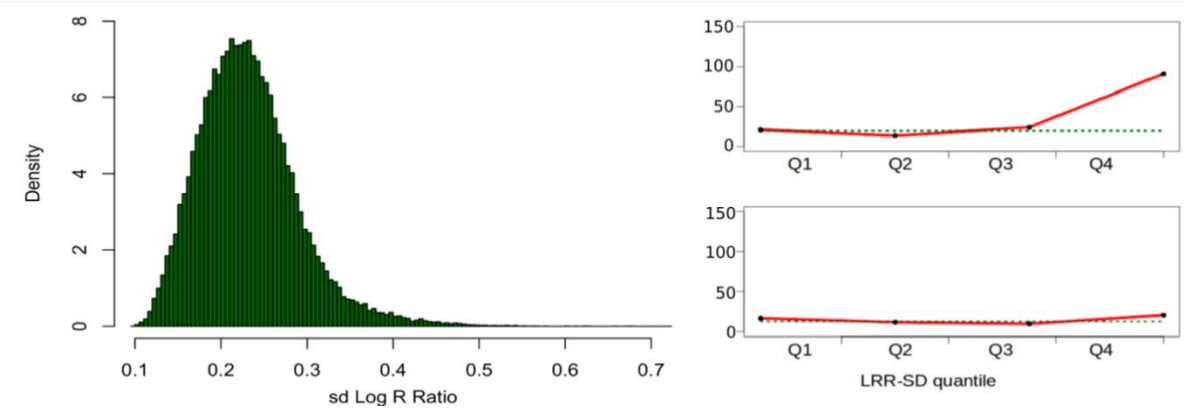
eTable 6. Somatic disorders observed in CNV carriers

			DELETIONS						
						Non-carrier	Carrier	Non-carrier	Carrier
Diagnosis	Locus	HR	Lower CI	UpperCI	P-value	w/o dx	w/o dx	w. dx	w. dx
Febrile seizures	15q11.2	0.48	0.21	1.07	0.070	62770	344	2881	8
Facial dysmorphism		0.50	0.16	1.56	0.23	64417	349	1234	<5
Infection (Genital)		0.83	0.26	2.58	0.74	64929	349	722	<5
Syncope		0.88	0.50	1.5	0.64	62846	339	2805	13
infection (Gastrointest)		0.93	0.65	1.3	0.69	58266	315	7385	37
Infection (Respiratory)		1.14	0.88	1.49	0.30	52466	271	13185	81
Infection (Otitis)		1.09	0.75	1.586	0.65	59531	318	6120	34
Infection (Skin)		1.24	0.86	1.79	0.25	60850	323	4801	29
Asthma		1.24	0.91	1.68	0.18	58267	307	7384	45
Infection (Urological)		1.50	0.88	2.55	0.13	63564	338	2087	14
Cardiac malformations		1.64	0.53	5.08	0.39	64764	347	887	5
Infection (Sepsis)		2.21	0.71	6.93	0.17	65200	348	451	<5
Infection (CNS)		2.31	0.96	5.58	0.062	65126	346	525	6
Juvenile arthritis		4.26	1.76	10.38	0.0014	65426	347	225	5
Thrombocytopenic purp		4.73	1.16	19.29	0.03	65572	350	79	<5
Asthma	15q13.3	0.77	0.25	2.39	0.65	63810	34	8029	<5
Infection (Skin)		0.76	0.18	3.09	0.70	66537	34	5302	<5
Syncope		1.06	0.27	4.2	0.93	68737	35	3102	<5
infection (Gastrointest)		1.23	0.54	2.84	0.61	63757	32	8082	5
Infection (Respiratory)		1.41	0.69	2.89	0.34	57364	29	14475	8
Infection (Otitis)		1.45	0.55	3.84	0.45	65150	32	6689	5
Infection (Urological)		1.71	0.45	6.45	0.43	69562	35	2277	<5
Facial dysmorphism		2.94	0.74	11.66	0.12	70488	35	1351	<5
Thyroiditis		44.7	10.8	185	2.1E-07	71756	35	83	<5
Infection (Skin)	16p11.2	0.86	0.21	3.49	0.83	51802	35	3999	<5
Syncope		-	-	-	-	-	-	-	-
Infection (Respiratory)		1.54	0.76	3.14	0.23	44612	30	11189	9
Febrile seizures		2.24	0.72	6.96	0.16	53319	34	2482	5
Asthma		2.38	1.19	4.74	0.014	49461	30	6340	9
infection (Gastrointest)		2.14	0.99	4.59	0.05	49598	31	6203	8
Infection (Otitis)	17p12	0.49	0.067	3.64	0.48	68249	29	7023	<5
infection (Gastrointest)		0.61	0.14	2.49	0.49	66821	29	8451	<5
Asthma		1.39	0.52	3.74	0.51	66857	27	8415	<5
Infection (Respiratory)		1.67	0.77	3.62	0.19	60087	23	15185	8

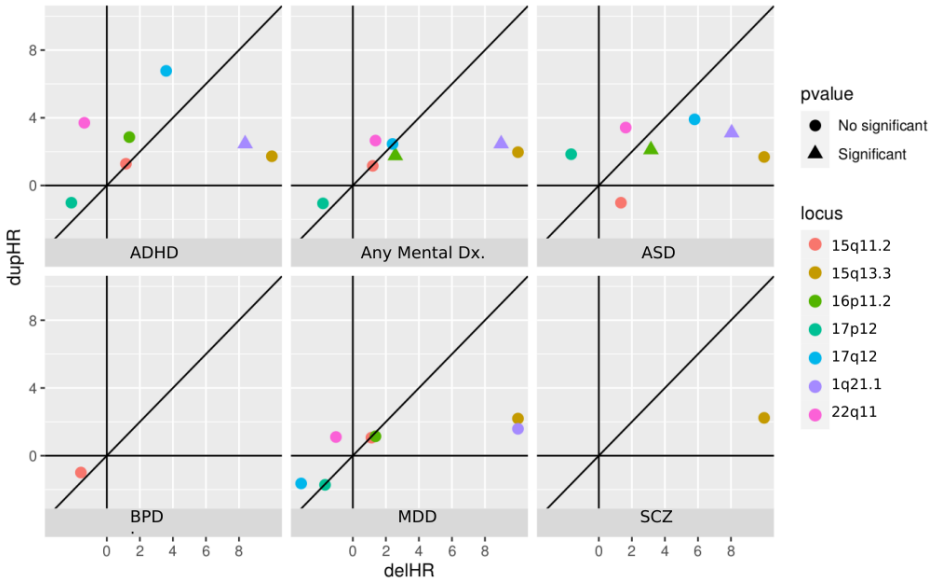
Infection (Respiratory)	17q12	-	-	-	-	-	-	-	-
Infection (Skin)		-	-	-	-	-	-	-	-
Asthma		1.71	0.55	5.26	0.35	58000	17	7360	<5
Infection (Otitis)		1.4	0.36	5.49	0.63	59216	17	6144	<5
Syncope		-	-	-	-	-	-	-	-
infection (Gastrointest.)		3.41	1.46	7.9	0.0045	58048	14	7312	7
Febrile seizures		4.21	1.42	12.5	0.0095	62478	17	2882	<5
Asthma	1q21.1	0.43	0.10	1.75	0.24	62225	43	7856	<5
Febrile seizures		0.58	0.080	4.23	0.59	66987	45	3094	<5
Infection (Skin)		0.65	0.16	2.65	0.55	64928	43	5153	<5
infection (Gastrointest)		0.87	0.34	2.25	0.78	62182	42	7899	5
Infection (Respiratory)		0.92	0.40	2.11	0.85	55980	37	14101	10
Syncope		1.51	0.51	4.48	0.46	67063	44	3018	<5
Infection (Otitis)		2.41	1.19	4.90	0.015	63588	38	6493	9
Infection (Sepsis)		5.40	0.74	39.32	0.096	69596	45	485	<5

			DUPLICATIOS						
						Non-carrier	Carrier	Non-carrier	Carrier
Diagnosis	Locus	HR	Lower C.I.	Upper C.I.	Pval	w/o dx	w/o dx	w. dx	w. dx
Syncope	15q11.2	0.69	0.37	1.29	0.25	62846	331	2805	10
Infection (Urological)		0.73	0.35	1.52	0.40	63564	333	2087	8
Facial dysmorphism		0.88	0.36	2.12	0.77	64417	334	1234	7
Infection (CNS)		0.97	0.24	3.9	0.97	65126	338	525	<5
Asthma		1.03	0.73	1.44	0.87	58267	302	7384	39
Infection (Genital)		1.12	0.42	2.93	0.82	64929	337	722	<5
Cardiac malformations		1.14	0.286	4.6	0.84	64764	338	887	<5
Infection (Otitis)		1.19	0.82	1.73	0.35	59531	305	6120	36
Infection (Respiratory)		1.24	0.95	1.61	0.11	52466	256	13185	85
Infection (Gastrointest)		1.26	0.93	1.72	0.13	58266	297	7385	44
Infection (Skin)		1.38	0.96	1.98	0.080	60850	308	4801	33
Febrile seizures		1.39	0.85	2.28	0.18	62770	319	2881	22
Ulcerative colitis		2.34	0.75	7.25	0.14	65382	338	269	<5
Infection (Sepsis)		2.42	0.77	7.54	0.13	65200	338	451	<5
Infection (Hepatitis)		2.91	0.73	11.59	0.13	65510	338	141	<5
Asthma	15q13.3	0.57	0.21	1.51	0.26	63810	66	8029	6
Infection (Otitis)		0.95	0.40	2.3	0.92	65150	66	6689	6
Infection (Respiratory)		0.96	0.52	1.78	0.91	57364	57	14475	15
Infection (Gastrointest)		1.15	0.57	2.33	0.68	63757	63	8082	9
Febrile seizures		1.26	0.40	3.98	0.69	68661	66	3178	6
Infection (Skin)		1.81	0.93	3.53	0.078	66537	62	5302	10
Facial dysmorphism		2.46	0.79	7.71	0.12	70488	69	1351	<5
Infection (Skin)	16p11.2	0.8	0.36	1.78	0.59	51802	102	3999	7
Infection (Gastrointest)		0.64	0.30	1.35	0.24	49598	101	6203	8
Infection (Respiratory)		0.85	0.49	1.47	0.56	44612	86	11189	23
Asthma		0.72	0.36	1.44	0.35	49461	99	6340	10
Syncope		0.61	0.19	1.92	0.40	53474	106	2327	<5

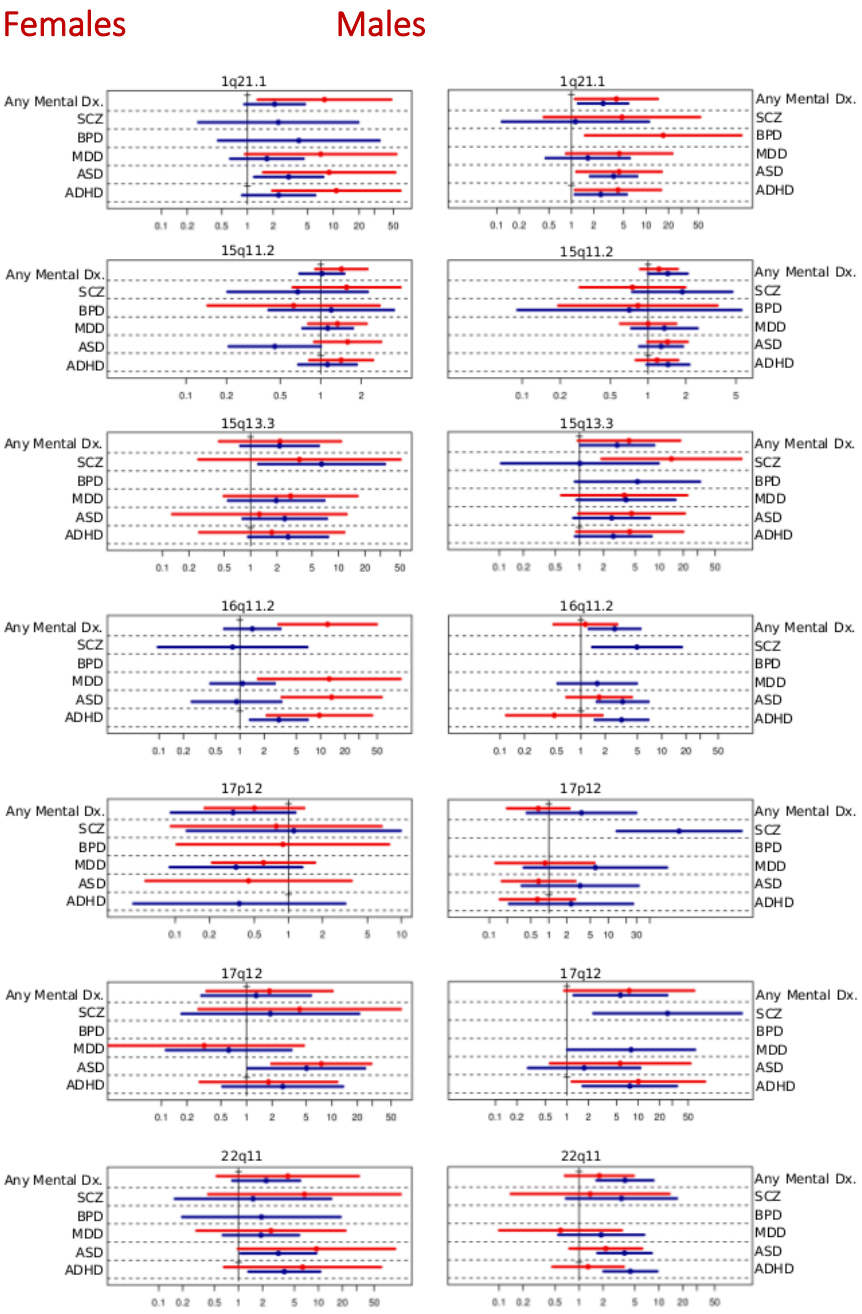
Facial dysmorphism		1.55	0.50	4.77	0.44	54753	106	1048	<5
Infection (Otitis)		1.73	1.04	2.85	0.033	50542	91	5259	18
Infection (Urological)		2.10	0.95	4.67	0.067	54082	102	1719	7
Infection (Genital)		2.59	0.81	8.22	0.11	55226	106	575	<5
Febrile seizures		2.71	1.51	4.88	0.00089	53319	97	2482	12
Infection (CNS)		-	-	-	-	-	-	-	-
Asthma	17p12	-	-	-	-	-	-	-	-
Infection (Otitis)		0.90	0.13	6.40	0.92	68249	15	7023	<5
Infection (Respiratory)		1.84	0.71	4.74	0.21	60087	11	15185	6
Infection (Skin)		0.98	0.14	6.98	0.98	69708	15	5564	<5
Infection (Urological)		-	-	-	-	-	-	-	-
Infection (Gastrointest)		4.4	1.96	9.88	0.00032	66821	11	8451	6
Syncope		4.23	1.32	13.6	0.015	72027	14	3245	<5
Infection (Skin)	17q12	0.78	0.19	3.26	0.74	60609	34	4751	<5
Infection (Respiratory)		1.00	0.42	2.37	0.99	52207	27	13153	9
Asthma		1.14	0.42	3.13	0.79	58000	32	7360	<5
Syncope		1.23	0.31	4.89	0.76	62574	34	2786	<5
Infection (Otitis)		1.52	0.56	4.15	0.41	59216	30	6144	6
Infection (Gastrointest)		1.82	0.82	4.03	0.14	58048	29	7312	6
Facial dysmorphism		1.65	0.24	11.5	0.61	64128	34	1232	<5
Febrile seizures		3.07	1.16	8.09	0.023	62478	31	2882	5
Infection (Urological)	1q21.1	0.44	0.06	3.03	0.41	67861	95	2220	<5
Infection (Gastrointest)		0.81	0.38	1.72	0.59	62182	88	7899	9
Syncope		1.08	0.41	2.86	0.87	67063	93	3018	<5
Asthma		1.08	0.57	2.04	0.80	62225	85	7856	12
Infection (Skin)		1.20	0.57	2.53	0.63	64928	89	5153	8
Infection (Respiratory)		1.43	0.89	2.29	0.13	55980	71	14101	26
Infection (Otitis)		1.48	0.82	2.67	0.19	63588	84	6493	13
Febrile seizures		1.97	0.93	4.15	0.075	66987	88	3094	9



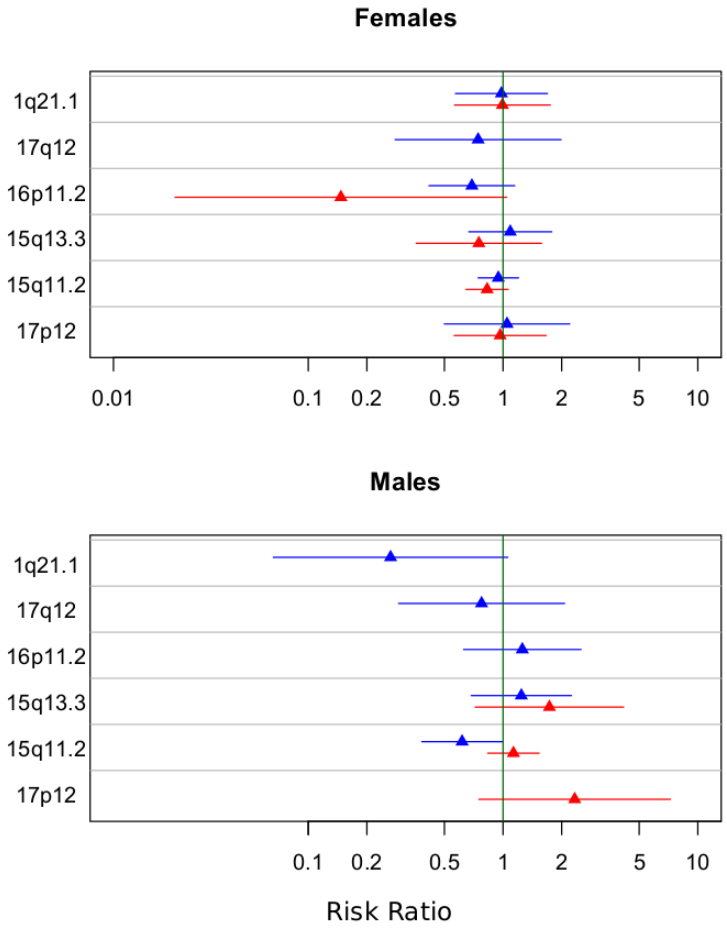
eFigure 1. CNV calling QC. A. Distribution of the sd Log R Ratio in the iPSYCH cohort. B. Quantile based quality control. Example of deletion at 16p11.2 locus. Top image: calls per Log R Ratio sd quantile before filtering noisy samples, bottom image: calls per Log R Ratio sd quantile after removing noisy samples.



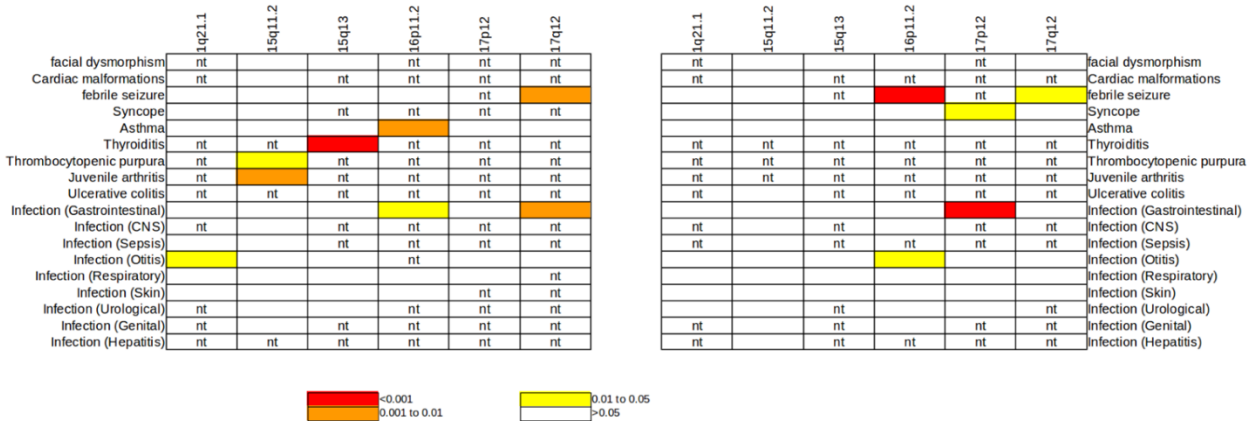
eFigure 2. Within CNV-locus comparison of deletion and duplication. For each mental disorder, the hazard ratio of the deletion (X-axis; delHR) and the duplication (Y-axis; dupHR) is plotted for each of the seven CNV-loci. The diagonal, corresponding to identical hazard ratio for deletion and duplication, is shown as a black line. CNV-loci with nominally different hazard ratios for deletions and duplication are shown as triangles while non-significant loci are shown as circles.



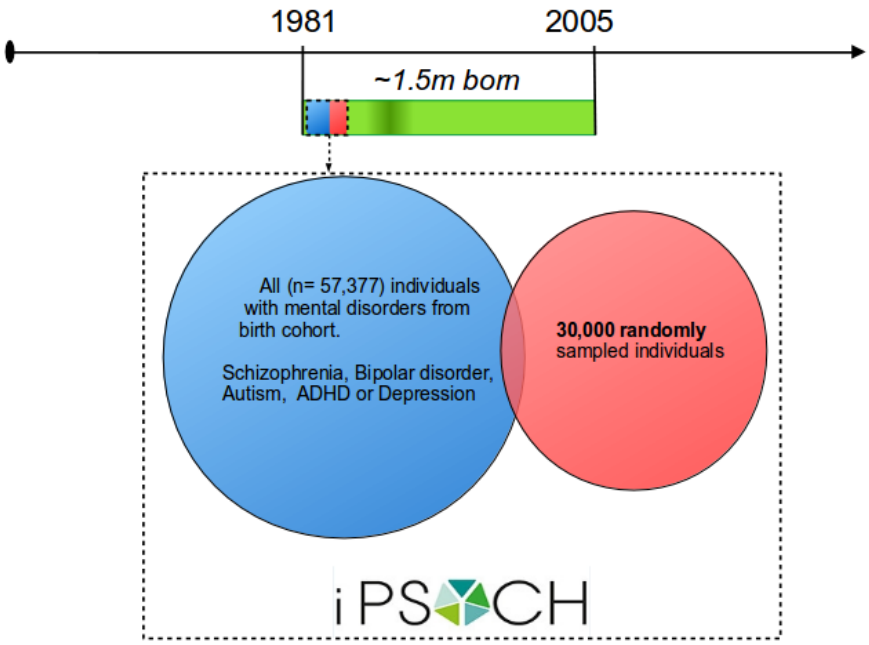
eFigure 3. Gender-stratified hazard ratio (HR) for mental disorders. Hazard ratios and CI95% (shown in logarithmic scale) are computed using a Cox-regression model for each locus left and right panels showing results for females and males respectively. Red and blue estimates denote deletions and duplications, respectively. Note, x-axis differs across loci.



eFigure 4. Fertility: CNV effect on number of children. Risk ratio (RR) and 95% confidence interval indicating the relative change in number of offspring carriers of a CNV vs subjects without CNV, in the entire iPSYCH sample. The risk ratio is derived from a Poisson regression model with age and mental disorders as covariates, and done separately for male and female subjects. Red indicates deletions and blue duplications. Comparable



eFigure 5. Somatic disorders enriched in individuals with CNVs. Somatic disorders, observed in a least two carriers with a given CNV and enriched in the CNV carriers relative to the background population based on Cox regression model. P-values are uncorrected. nt = not tested.



eFigure 6. iPSYCH study design Venn diagram.

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