

SUPPLEMENTARY INFORMATION

Impact of Copy Number Variants and Polygenic Risk Scores on Psychopathology in the UK Biobank

Mollon et al.

Table S1 List of 61 recurrent CNVs selected for analyses

Locus	Gene(s)	CHR	hg19 START	hg19 STOP
1p36	<i>GABRD</i>	chr1	1	2500000
1q21.1 TAR	-	chr1	145394955	145807817
1q21.1 distal+TAR	-	chr1	145394955	147394444
1q21.1 distal	-	chr1	146527987	147394444
-	<i>NRXN1</i>	chr2	50145643	51259674
2q11.2	<i>ARID5A, LMAN2L</i>	chr2	96742409	97677516
2q13	<i>NPHP1</i>	chr2	110862716	110983948
2q13	<i>BUB1</i>	chr2	111394040	112012649
2q21.1	-	chr2	131481308	131930677
2q37	<i>HDAC4</i>	chr2	239716679	243199373
3q29 proximal	<i>FGF12</i>	chr3	191517306	193017306
3q29 distal	<i>DLG1</i>	chr3	195720167	197354826
4p16.3 (WH)	-	chr4	1552030	2091303
5q35	-	chr5	175720924	177052594
-	<i>SIM1</i>	chr6	100836750	100911811
-	<i>ZNF92</i>	chr7	64838768	64865998
7q11.23 (WBS)	<i>GTF2I, GTF2IRD1</i>	chr7	72744915	74142892
7q11.23 proximal	-	chr7	73978801	74144177
7q11.23	<i>WBSCR16</i>	chr7	74455447	74488775
7q11.23 distal	-	chr7	75138294	76064412
7p36.3	<i>VIPR2, WDR60</i>	chr7	158660506	159179546
8p23.1	-	chr8	8098990	11872558
-	<i>VPS13B</i>	chr8	100025494	100889808
-	<i>DMRT1</i>	chr9	841690	969090
9q34	<i>EHMT1</i>	chr9	140513444	140730578
10q11.21q11.23	-	chr10	49390199	51058796
10q22q23	<i>GRID1, NRG3</i>	chr10	82045472	88931651
11p11.2	-	chr11	43940000	46020000
-	<i>ZMYM5</i>	chr13	20411593	20437773
-	<i>CRYL1</i>	chr13	20977806	21100012
13q12.12	-	chr13	23555358	24884622
15q11.2	-	chr15	22805313	23094530
15q11.2q13.1 BP2-BP3 (PWS/AS)	-	chr15	22805313	28390339
15q12	<i>GABRA5, GABRB3, GABRG3</i>	chr15	26971834	27548820
15q13.1q13.2 BP3-BP4	-	chr15	29161368	30375967
15q13.1q13.3 BP3-BP5	-	chr15	29161368	32462776
15q13.3 BP4-BP5	<i>CHRNA7</i>	chr15	31080645	32462776
15q13.3 BP4.5-BP5	<i>CHRNA7</i>	chr15	32017070	32453068
15q24	-	chr15	72900171	78151253
15q25.2	-	chr15	83219735	85722039
-	<i>CREBBP</i>	chr16	3775056	3930121
16p13.11	-	chr16	15511655	16293689
16p12.1	-	chr16	21950135	22431889
16p11.2 distal	-	chr16	28823196	29046783
16p11.2 distal+proximal	-	chr16	28823196	30200773
16p11.2 proximal	-	chr16	29650840	30200773
16p11.2p12.1	-	chr16	21596415	28347808
16q23.3	<i>CDH13</i>	chr16	82660399	83830215
-	<i>YWHAE</i>	chr17	1247834	1303556
-	<i>PAFAH1B1</i>	chr17	2496923	2588909
17p12	<i>PMP22</i>	chr17	14141387	15426961
17p11.2 (Potocki-Lupski/SMS)	-	chr17	16812771	20211017
17q11.2	<i>NF1</i>	chr17	29107491	30265075
17q12	-	chr17	34815904	36217432
17q21.31	-	chr17	43705356	44164691
17q23.1q23.2	-	chr17	58302389	60289141
22q11.2 distal	-	chr22	21920127	23653646
22q11.2 proximal	-	chr22	19037332	21466726
22q13	<i>SHANK3</i>	chr22	51113070	51171640
-	<i>MAGEA11</i>	chrX	148793685	148798928
Xq28	-	chrX	154146806	154571806

TAR = thrombocytopenia-absent radius; WH = Wolf-Hirschhorn; WBS = Williams-Beuren syndrome; PWS/AS = Prader-Willi syndrome / Angelman syndrome; SMS = Smith-Magenis syndrome.

Table S2 Items and factor loadings for mood/anxiety confirmatory factor model (N=501,289)

Touchscreen question	Loading
Over the past two weeks, how often have you felt down, depressed, or hopeless?	0.858
Does your mood often go up and down?	0.804
Do you often feel 'fed-up'?	0.803
Over the past two weeks, how often have you had little interest or pleasure in doing things?	0.770
Do you ever feel 'just miserable' for no reason?	0.761
Over the past two weeks, how often have you felt tense, fidgety or restless?	0.761
Would you call yourself tense or 'highly strung'?	0.726
Would you call yourself a nervous person?	0.716
Are you a worrier?"	0.696
Do you suffer from 'nerves'?	0.685
Do you often feel lonely?	0.670
Are you often troubled by feelings of guilt?	0.638
Are your feelings easily hurt?	0.624
Do you worry too long after an embarrassing experience?	0.609
Are you an irritable person?	0.588
Over the past two weeks, how often have you felt tired or had little energy?	0.587

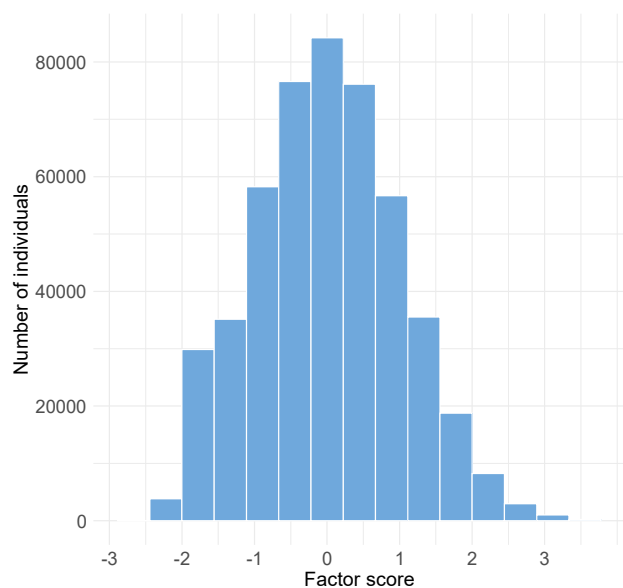
Figure S1 Distribution of mood/anxiety factor

Table S3 ICD-10 diagnoses and codes

Diagnosis	Code(s)	N
Dementia	F00-F03	2,041
Delirium	F05	1,559
Substance use	F10-F19	23,909
Psychosis	F20-F29	1,546
Mania	F30	230
Bipolar	F31	1,447
Depression	F32	19,101
Recurrent depression	F33	997
Other mood	F34-39	183
Anxiety	F40-F48	10,544
Eating	F50	137
Sleep	F51	72
Personality	F60	487
Mental retardation	F70-F79	101
Development	F80-F89	519
Behavioral	F90-F98	64
Unspecified	F99	287
Any	F00-F99	50,501

ICD-10 = International Statistical Classification of Diseases and Related Health Problems, Tenth Revision

Table S4 Sensitivity analyses: Standardized mean differences between CNV carriers and non-carriers on mood/anxiety factor scores for individuals of White British ancestry

CNV	Category	N	β	SE	p
Any CNV	Intolerant	33,158	0.055	0.006	$<2 \times 10^{-16}$
	Recurrent	14,355	0.084	0.008	$<2 \times 10^{-16}$
	Intolerant recurrent	8,363	0.122	0.011	$<2 \times 10^{-16}$
	Recurrent rare	6,020	0.146	0.013	$<2 \times 10^{-16}$
	Intolerant recurrent rare	5,145	0.156	0.014	$<2 \times 10^{-16}$
Any deletion	Intolerant	7,598	0.115	0.011	$<2 \times 10^{-16}$
	Recurrent	5,666	0.138	0.013	$<2 \times 10^{-16}$
	Intolerant recurrent	2,808	0.199	0.018	$<2 \times 10^{-16}$
	Recurrent rare	2,235	0.166	0.021	1×10^{-15}
	Intolerant recurrent rare	1,462	0.195	0.026	3×10^{-14}
Any duplication	Intolerant	25,560	0.037	0.006	3×10^{-9}
	Recurrent	8,547	0.047	0.011	$<2 \times 10^{-16}$
	Intolerant recurrent	5,441	0.082	0.013	7×10^{-10}
	Recurrent rare	3,764	0.134	0.016	$<2 \times 10^{-16}$
	Intolerant recurrent rare	3,662	0.139	0.016	$<2 \times 10^{-16}$

β coefficients correspond to standardized effect sizes, with values of 0.2, 0.5, and 0.8 indicating small, medium, and large effects, respectively.

Intolerant = CNV risk score (CRS) >2.86 ; Recurrent = any of the 61 neuropsychiatric recurrent CNVs; Intolerant recurrent = any of the 61 neuropsychiatric recurrent CNVs with a CRS >2.86 ; Recurrent rare = any of the 57 rare neuropsychiatric recurrent CNVs i.e., excluding the high frequency 2q13 (NPHP1), 15q11.2, 15q13.3 (CHRNA7), and ZNF92 CNVs; Intolerant recurrent rare = any of the 57 rare neuropsychiatric recurrent CNVs with a CRS >2.86 (i.e., excluding the high frequency 2q13 (NPHP1), 15q11.2, 15q13.3 (CHRNA7)).

Table S5 Sensitivity analyses: Standardized mean differences between CNV carriers and non-carriers on mood/anxiety factor scores for individuals without ICD psychiatric diagnoses

CNV	Category	N	β	SE	p
Any CNV	Intolerant	30,935	0.040	0.006	2×10^{-12}
	Recurrent	14,991	0.067	0.008	$<2 \times 10^{-16}$
	Intolerant recurrent	8,524	0.096	0.010	$<2 \times 10^{-16}$
	Recurrent rare	5,396	0.120	0.013	$<2 \times 10^{-16}$
	Intolerant recurrent rare	4,590	0.126	0.014	$<2 \times 10^{-16}$
Any deletion	Intolerant	6,915	0.087	0.012	4×10^{-14}
	Recurrent	5,765	0.116	0.012	$<2 \times 10^{-16}$
	Intolerant recurrent	2,800	0.167	0.018	$<2 \times 10^{-16}$
	Recurrent rare	1,965	0.132	0.022	1×10^{-9}
	Intolerant recurrent rare	1,259	0.151	0.027	2×10^{-8}
Any duplication	Intolerant	24,020	0.026	0.006	5×10^{-5}
	Recurrent	9,100	0.035	0.010	5×10^{-4}
	Intolerant recurrent	5,621	0.059	0.013	5×10^{-6}
	Recurrent rare	3,418	0.114	0.016	4×10^{-12}
	Intolerant recurrent rare	3,318	0.117	0.017	2×10^{-12}

β coefficients correspond to standardized effect sizes, with values of 0.2, 0.5, and 0.8 indicating small, medium, and large effects, respectively.

Intolerant = CNV risk score (CRS) >2.86 ; Recurrent = any of the 61 neuropsychiatric recurrent CNVs; Intolerant recurrent = any of the 61 neuropsychiatric recurrent CNVs with a CRS >2.86 ; Recurrent rare = any of the 57 rare neuropsychiatric recurrent CNVs i.e., excluding the high frequency 2q13 (NPHP1), 15q11.2, 15q13.3 (CHRNA7), and ZNF92 CNVs; Intolerant recurrent rare = any of the 57 rare neuropsychiatric recurrent CNVs with a CRS >2.86 (i.e., excluding the high frequency 2q13 (NPHP1), 15q11.2, 15q13.3 (CHRNA7)).

Table S6 Associations between individual recurrent deletions and mood/anxiety factor

Deletion	All participants					White British				Excluding psychiatric diagnoses			
	CRS	N	β	SE	p	N	β	SE	p	N	β	SE	p
22q11.2 proximal with LCR-A	64.06	10	0.959	0.310	0.002	10	0.952	0.308	0.002	6	0.294	0.388	0.449
10q11.21q11.23	28.62	61	0.503	0.125	6×10⁻⁵	54	0.586	0.133	1×10⁻⁵	54	0.464	0.129	3×10⁻⁴
15q13.1q13.3 BP3-BP5	8.69	58	0.416	0.129	0.001	47	0.416	0.142	0.003	42	0.429	0.147	0.003
16p13.11	24.21	138	0.392	0.083	0.000	117	0.361	0.090	0.000	105	0.321	0.093	0.001
16p11.2 distal BP2-BP3	21.39	58	0.340	0.130	0.009	51	0.380	0.136	0.005	46	0.333	0.142	0.019
22q11.2 distal type II	9.57	46	0.323	0.144	0.025	40	0.351	0.154	0.023	38	0.316	0.154	0.040
ZMYM5	0.96	6	0.306	0.400	0.445	-	-	-	-	5	0.013	0.425	0.976
17q12	37.34	8	0.290	0.346	0.402	6	0.374	0.398	0.347	6	0.483	0.388	0.214
15q13.3 (<i>CHRNA7</i>)	1.30	8	0.284	0.346	0.413	8	0.289	0.345	0.402	6	-0.129	0.388	0.740
2q21.1 (<i>BUB1</i>)	5.81	44	0.277	0.148	0.061	38	0.207	0.158	0.191	40	0.326	0.150	0.030
16p12.1	9.03	255	0.258	0.061	3×10⁻⁵	228	0.247	0.065	1×10⁻⁴	208	0.200	0.066	0.002
16p11.2 proximal BP4-BP5	40.03	126	0.225	0.088	0.011	96	0.298	0.100	0.003	85	0.207	0.104	0.047
1q21.1 distal TAR	19.70	11	0.211	0.295	0.475	10	0.192	0.308	0.534	8	0.425	0.336	0.206
15q11.2	6.91	1746	0.189	0.024	1×10⁻⁵	1553	0.195	0.025	4×10⁻¹⁵	1573	0.177	0.024	2×10⁻¹³
22q11.2 proximal without LCR-A	10.53	36	0.177	0.163	0.279	27	0.131	0.188	0.485	26	-0.060	0.187	0.749
<i>NRXN1</i>	3.94	287	0.164	0.058	0.005	247	0.175	0.062	0.005	253	0.154	0.060	0.010
2q11.2	44.46	34	0.134	0.168	0.424	28	0.113	0.184	0.541	30	0.071	0.174	0.683
<i>PAFAH1B1</i>	16.03	6	0.125	0.400	0.754	5	0.175	0.436	0.688	6	0.184	0.388	0.635
<i>CRYL1</i>	1.52	401	0.125	0.049	0.011	360	0.118	0.051	0.021	357	0.107	0.050	0.034
17p12 (<i>HNPP, CMT1A</i>)	8.63	263	0.084	0.060	0.165	220	0.082	0.066	0.212	234	0.063	0.062	0.313
2q13 (<i>NPHP1</i>)	1.74	2617	0.066	0.019	0.001	2259	0.069	0.021	0.001	2342	0.061	0.020	0.002
1q21.1 distal	10.44	107	0.049	0.095	0.602	93	-0.020	0.101	0.845	94	0.039	0.098	0.694
13q12.12	8.78	86	0.049	0.106	0.641	79	0.079	0.110	0.472	80	0.108	0.106	0.310
<i>SIM1</i>	3.95	6	0.049	0.400	0.903	5	0.393	0.436	0.367	5	-0.293	0.425	0.491
<i>VPS13B</i>	1.54	38	0.043	0.159	0.787	33	-0.055	0.170	0.748	32	0.012	0.168	0.942
3q29 distal	41.32	10	0.014	0.310	0.963	9	-0.104	0.325	0.749	-	-	-	-
<i>ZNF92</i>	0.54	3274	0.011	0.017	0.527	2639	0.016	0.019	0.399	2924	0.006	0.018	0.742
1q21.1 TAR	19.70	151	-0.019	0.080	0.810	130	0.058	0.085	0.497	140	-0.049	0.080	0.539
17q11.2 (<i>NF1</i>)	35.36	12	-0.031	0.283	0.913	10	-0.107	0.308	0.729	12	0.027	0.275	0.922
2q13	15.84	60	-0.034	0.126	0.786	54	-0.060	0.133	0.649	54	-0.085	0.129	0.510
15q13.1q13.2 BP3-BP4	20.13	10	-0.073	0.326	0.823	9	-0.065	0.325	0.841	7	-0.193	0.359	0.592
16q23.3	2.39	18	-0.104	0.231	0.651	13	-0.418	0.270	0.122	16	-0.100	0.238	0.675
<i>DMRT1</i>	6.07	16	-0.243	0.245	0.322	13	-0.159	0.270	0.556	16	-0.183	0.238	0.442
4p16.3	7.18	6	-0.413	0.400	0.302	5	-0.117	0.436	0.788	-	-	-	-

β coefficients correspond to standardized effect sizes, with values of 0.2, 0.5, and 0.8 indicating small, medium, and large effects, respectively.

Bolded estimates signify statistical significance ($p_{FDR} < 0.05$).

CRS = CNV risk score; LCR = low-copy repeat; BP = breakpoint; TAR = thrombocytopenia-absent radius.

Table S7 Associations between individual recurrent duplications and mood/anxiety factor

Duplication	All participants					White British				Excluding psychiatric diagnoses			
	CRS	N	β	SE	<i>p</i>	N	β	SE	<i>p</i>	N	β	SE	<i>p</i>
8p23.1	12.75	7	1.087	0.370	0.003	6	1.241	0.398	0.002	5	1.278	0.425	0.003
15q11.2q13.1 BP2-BP3 PWS/AS	31.73	19	0.936	0.225	3×10⁻⁵	17	0.865	0.236	3×10⁻⁴	11	0.804	0.287	0.005
3q29 proximal	7.14	7	0.790	0.370	0.033	6	0.897	0.398	0.024	7	0.851	0.359	0.018
10q22q23 (<i>NRG3, GRID1</i>)	44.32	8	0.744	0.346	0.032	7	0.771	0.368	0.036	7	0.650	0.359	0.071
22q11.2 proximal with LCR-A	76.42	287	0.545	0.058	2×10⁻¹⁶	254	0.552	0.061	2×10⁻¹⁶	249	0.525	0.060	0.000
16p11.2 proximal BP4-BP5	40.03	147	0.435	0.081	8×10⁻⁸	135	0.418	0.084	6×10⁻⁷	122	0.360	0.086	0.000
1q21.1 distal TAR	31.89	20	0.433	0.219	0.048	15	0.439	0.252	0.081	17	0.268	0.231	0.245
15q24	25.47	9	0.418	0.326	0.201	8	-0.496	0.345	0.150	7	0.534	0.359	0.137
7q11.23 WBS	51.74	17	0.360	0.237	0.129	13	0.528	0.270	0.051	15	-0.255	0.246	0.299
1q21.1 distal	10.44	169	0.359	0.075	2×10⁻⁶	148	0.390	0.080	1×10⁻⁶	145	0.332	0.079	0.000
16p11.2 distal BP2-BP3	21.93	115	0.255	0.091	0.005	105	0.244	0.095	0.010	95	0.269	0.098	0.006
4p16.3	7.18	11	0.200	0.295	0.499	9	0.029	0.325	0.928	9	0.081	0.317	0.798
17p12 (<i>HNPP, CMT1A</i>)	8.63	137	0.171	0.084	0.040	116	0.206	0.090	0.023	111	0.145	0.090	0.108
15q13.3 BP4-BP5 (<i>CHRNA7</i>)	8.69	65	0.159	0.121	0.189	56	-0.263	0.130	0.044	58	0.147	0.125	0.238
15q13.1q13.3 BP3-BP5	8.69	250	0.158	0.062	0.011	214	0.109	0.067	0.102	223	0.139	0.064	0.029
1q21.1 TAR	19.70	442	0.148	0.047	0.002	388	0.129	0.049	0.009	390	0.135	0.048	0.005
22q11.2 distal type III	30.85	208	0.140	0.068	0.040	178	0.158	0.073	0.030	181	0.104	0.071	0.143
22q11.2 distal type II	9.57	49	0.124	0.141	0.382	47	0.083	0.142	0.561	38	0.023	0.156	0.884
2q21.1 (<i>BUB1</i>)	5.81	62	0.089	0.124	0.474	54	0.108	0.133	0.416	59	0.119	0.124	0.335
16p12.1	9.03	196	0.057	0.070	0.418	173	0.057	0.074	0.442	178	0.077	0.071	0.278
17q12	37.08	105	0.055	0.096	0.564	95	0.085	0.100	0.397	90	0.004	0.100	0.965
<i>ZNF92</i>	0.54	237	0.047	0.064	0.465	202	0.075	0.069	0.274	214	0.089	0.065	0.173
2q13	15.11	74	0.041	0.114	0.718	68	0.028	0.118	0.816	67	0.023	0.116	0.843
2q11.2	44.46	32	0.029	0.173	0.868	28	0.083	0.184	0.651	28	0.037	0.180	0.837
7q11.23 distal	9.17	29	0.010	0.182	0.954	22	-0.045	0.208	0.829	29	0.068	0.177	0.698
15q13.3 (<i>CHRNA7</i>)	1.30	3089	0.005	0.018	0.790	2660	0.003	0.019	0.874	2819	0.009	0.018	0.626
16p13.11	23.67	890	-0.007	0.033	0.842	775	-0.021	0.035	0.553	795	-0.007	0.034	0.834
2q13 (<i>NPHP1</i>)	1.74	1117	-0.021	0.029	0.480	784	-0.043	0.035	0.216	1004	-0.023	0.030	0.442
22q11.2 proximal without LCR-A	23.36	209	-0.024	0.068	0.728	178	-0.027	0.073	0.707	188	-0.039	0.069	0.573
15q11.2	6.91	2268	-0.027	0.021	0.193	1849	-0.008	0.023	0.735	2003	-0.032	0.021	0.132
<i>ZMYM5</i>	6.48	81	-0.028	0.109	0.796	66	-0.074	0.120	0.538	71	-0.046	0.113	0.681
13q12.12	8.78	255	-0.037	0.061	0.545	221	-0.055	0.066	0.401	228	-0.097	0.063	0.124
10q11.21q11.23	33.70	44	-0.051	0.148	0.729	38	-0.037	0.158	0.815	39	-0.024	0.152	0.876
16q23.3	2.39	61	-0.052	0.125	0.676	55	-0.042	0.131	0.750	58	0.036	0.125	0.776
22q11.2 distal type I	25.86	9	-0.068	0.326	0.835	9	-0.068	0.325	0.835	8	-0.101	0.336	0.765
<i>YWHAE</i>	14.19	10	-0.080	0.310	0.797	9	-0.164	0.325	0.613	6	-0.582	0.388	0.134
<i>CRYL1</i>	3.43	5	-0.160	0.438	0.716	-	-	-	-	5	-0.098	0.425	0.818
17p11.2 Potocki-Lupski/SMS	22.51	6	-0.191	0.400	0.632	5	-0.106	0.436	0.808	-	-	-	-
16p11.2 distal BP1-BP2-BP3	31.26	12	-0.192	0.283	0.496	10	-0.377	0.308	0.221	10	-0.194	0.301	0.519
17q21.31	2.28	6	-0.369	0.400	0.356	6	-0.367	0.398	0.357	-	-	-	-
15q13.1q13.2 BP3-BP4	19.08	24	-0.374	0.200	0.062	20	-0.421	0.218	0.053	23	-0.341	0.198	0.086
<i>DMRT1</i>	5.32	16	-0.627	0.245	0.010	15	-0.588	0.252	0.019	16	-0.565	0.238	0.017
15q12 (<i>GABRB3, GABRA5</i>)	8.22	8	-0.666	0.346	0.054	7	-0.693	0.368	0.060	8	-0.728	0.336	0.030

β coefficients correspond to standardized effect sizes, with values of 0.2, 0.5, and 0.8 indicating small, medium, and large effects, respectively.

Bolded estimates signify statistical significance ($p_{FDR}<0.05$).

CRS = CNV risk score; LCR = low-copy repeat; BP = breakpoint; TAR = thrombocytopenia-absent radius; WH = Wolf-Hirschhorn; WBS = Williams-Beuren syndrome; PWS/AS = Prader-Willi syndrome / Angelman syndrome; SMS = Smith-Magenis syndrome.

Table S8 CNV×PRS interactions between individual recurrent deletions and MDD PRS

CNV	N	β	SE	<i>p</i>
15q13.3 (<i>CHRNA7</i>)	8	0.814	0.339	0.017
3q29 distal	9	0.424	0.442	0.338
<i>PAFAH1B1</i>	5	0.283	0.649	0.662
17q11.2 (<i>NF1</i>)	10	0.255	0.315	0.418
<i>SIM1</i>	5	0.208	0.601	0.729
2q21.1 (<i>BUB1</i>)	38	0.198	0.196	0.311
10q11.21q11.23	54	0.182	0.126	0.148
15q13.1q13.2 BP3-BP4	9	0.144	0.364	0.692
<i>VPS13B</i>	33	0.121	0.168	0.472
16p12.1	228	0.089	0.063	0.158
16p11.2 proximal BP4 BP5	96	0.082	0.098	0.401
17p12 (<i>HNPP</i> , <i>CMT1A</i>)	220	0.058	0.072	0.421
22q11.2 distal type II	40	0.043	0.124	0.728
1q21.1 distal	93	0.042	0.095	0.659
2q13	54	0.034	0.154	0.826
<i>CRYL1</i>	360	0.021	0.051	0.672
15q11.2	1553	0.010	0.025	0.692
<i>ZNF92</i>	2639	0.007	0.020	0.713
<i>DMRT1</i>	13	0.005	0.249	0.983
2q13 (<i>NPHP1</i>)	2259	-0.004	0.021	0.837
2q11.2	28	-0.027	0.167	0.874
<i>NRXN1</i>	247	-0.059	0.061	0.334
17q12	6	-0.062	0.513	0.904
16p11.2 distal BP2-BP3	51	-0.078	0.134	0.562
1q21.1 TAR	130	-0.085	0.089	0.339
13q12.12	79	-0.085	0.106	0.423
16p13.11	117	-0.095	0.090	0.291
16q23.3	13	-0.127	0.319	0.690
1q21.1 distal TAR	10	-0.134	0.308	0.664
22q11.2 proximal without LCR-A	27	-0.165	0.204	0.419
22q11.2 proximal with LCR-A	10	-0.216	0.371	0.560
15q13.1q13.3 BP3-BP5	47	-0.273	0.135	0.044
4p16.3	5	-0.527	0.483	0.275

MDD = major depressive disorder; PRS = polygenic risk score.

β coefficients correspond to standardized effect sizes, with values of 0.2, 0.5, and 0.8 indicating small, medium, and large effects.

Bolded estimates signify nominal significance ($p < 0.05$).

CRS = CNV risk score; LCR = low-copy repeat; BP = breakpoint; TAR = thrombocytopenia-absent radius.

Table S9 CNV×PRS interactions between individual recurrent duplications and MDD PRS

CNV	N	β	SE	p
15q24	8	0.655	0.572	0.252
<i>YWHAE</i>	9	0.487	0.267	0.068
1q21.1 distal TAR	15	0.372	0.303	0.219
17q21.31	6	0.233	0.489	0.633
10q11.21q11.23	38	0.158	0.169	0.350
2q21.1 <i>BUB1</i>	54	0.144	0.116	0.214
1q21.1 distal	148	0.127	0.079	0.110
15q12 (<i>GABRB3</i> , <i>GABRA5</i>)	7	0.108	0.336	0.748
22q11.2 distal type III	178	0.099	0.072	0.169
7q11.23 distal	22	0.095	0.246	0.699
8p23.1	6	0.086	0.466	0.853
<i>ZNF92</i>	202	0.051	0.073	0.481
17p12 (<i>HNPP</i> , <i>CMT1A</i>)	116	0.051	0.090	0.570
16p12.1	173	0.049	0.077	0.524
2q13 (<i>NPHP1</i>)	784	0.039	0.034	0.247
16p13.11	775	0.035	0.037	0.351
16q23.3	55	0.033	0.115	0.775
16p11.2 proximal BP4-BP5	135	0.028	0.080	0.728
<i>DMRT1</i>	15	0.025	0.241	0.916
15q13.1q13.3 BP3-BP5	214	0.016	0.069	0.820
1q21.1 TAR	388	0.015	0.050	0.769
15q13.3 (<i>CHRNA7</i>)	2660	0.008	0.020	0.700
22q11.2 distal type II	47	0.000	0.138	0.998
<i>ZMYM5</i>	66	0.000	0.134	1.000
15q11.2	1849	-0.014	0.023	0.544
16p11.2 distal BP2-BP3	105	-0.018	0.099	0.857
22q11.2 proximal without LCR-A	178	-0.020	0.077	0.792
13q12.12	221	-0.028	0.061	0.645
15q13.3 BP4-BP5 (<i>CHRNA7</i>)	56	-0.058	0.140	0.678
4p16.3	9	-0.092	0.349	0.791
17q12	95	-0.097	0.101	0.339
2q13	68	-0.120	0.122	0.324
16p11.2 distal BP1-BP2-BP3	10	-0.131	0.418	0.754
22q11.2 proximal with LCR-A	254	-0.136	0.063	0.031
15q13.1q13.2 BP3-BP4	20	-0.166	0.238	0.485
2q11.2	28	-0.219	0.135	0.105
7q11.23 WBS	13	-0.242	0.353	0.493
22q11.2 distal type I	9	-0.276	0.331	0.405
15q11.2q13.1 BP2 BP3 PWS/AS	17	-0.327	0.299	0.275
17p11.2 Potocki Lupski/SMS	5	-0.674	0.476	0.157
10q22q23 (<i>NRG3</i> , <i>GRID1</i>)	7	-0.691	0.517	0.181
3q29 proximal	6	-0.903	0.701	0.197

MDD = major depressive disorder; PRS = polygenic risk score.

β coefficients correspond to standardized effect sizes, with values of 0.2, 0.5, and 0.8 indicating small, medium, and large effects, respectively.

Bolded estimates signify nominal significance ($p < 0.05$).

CRS = CNV risk score; LCR = low-copy repeat; BP = breakpoint; TAR = thrombocytopenia-absent radius; WH = Wolf-Hirschhorn; WBS = Williams-Beuren syndrome; PWS/AS = Prader-Willi syndrome / Angelman syndrome; SMS = Smith-Magenis syndrome.

Table S10 CNV×PRS interactions between individual recurrent deletions and GAD PRS

CNV	N	β	SE	<i>p</i>
17q11.2 NF1	10	0.363	0.417	0.384
22q11.2 proximal with LCR-A	10	0.358	0.359	0.320
DMRT1	13	0.281	0.270	0.299
3q29 distal	9	0.257	0.291	0.376
15q13.3 BP4.5 BP5 CHRNA7	8	0.109	0.598	0.856
1q21.1 distal TAR	10	0.108	0.315	0.732
22q11.2 distal type II	40	0.104	0.158	0.509
2q13	54	0.084	0.163	0.605
10q11.21q11.23	54	0.064	0.116	0.579
16p12.1	228	0.061	0.067	0.367
CRYL1	360	0.020	0.054	0.718
15q11.2	1553	0.016	0.026	0.532
1q21.1 distal	93	0.011	0.106	0.919
16p13.11	117	0.001	0.086	0.995
ZNF92	2639	-0.005	0.019	0.790
16p11.2 distal BP2 BP3	51	-0.013	0.126	0.918
17q12	6	-0.017	0.459	0.970
2q13 NPHP1	2259	-0.026	0.021	0.213
17p12 HNPP CMT1A	220	-0.033	0.073	0.645
2q11.2	28	-0.060	0.166	0.719
NRXN1	247	-0.063	0.064	0.325
2q21.1 BUB1	38	-0.081	0.176	0.647
4p16.3	5	-0.091	0.341	0.790
16p11.2 proximal BP4 BP5	96	-0.118	0.094	0.209
1q21.1 TAR	130	-0.126	0.090	0.163
13q12.12	79	-0.179	0.125	0.154
22q11.2 proximal without LCR-A	27	-0.179	0.179	0.319
VPS13B	33	-0.182	0.187	0.330
16q23.3	13	-0.184	0.269	0.493
15q13.1q13.2 BP3 BP4	9	-0.278	0.432	0.519
15q13.1q13.3 BP3 BP5	47	-0.304	0.168	0.070
SIM1	5	-0.340	1.210	0.778
PAFAH1B1	5	-1.484	0.584	0.011

GAD = generalized anxiety disorder; PRS = polygenic risk score.

β coefficients correspond to standardized effect sizes, with values of 0.2, 0.5, and 0.8 indicating small, medium, and large effects, respectively.

Bolded estimates signify nominal significance ($p < 0.05$).

CRS = CNV risk score; LCR = low-copy repeat; BP = breakpoint; TAR = thrombocytopenia-absent radius.

Table S11 CNV×PRS interactions between individual recurrent duplications and GAD PRS

CNV	N	β	SE	<i>p</i>
17q21.31	6	0.613	0.661	0.354
15q12 GABRB3 GABRA5	7	0.603	0.513	0.240
YWHAE	9	0.375	0.339	0.268
15q13.3 BP4 BP5 CHRNA7	56	0.339	0.141	0.016
22q11.2 distal type II	47	0.262	0.155	0.091
15q11.2q13.1 BP2 BP3 PWS.AS	17	0.217	0.308	0.481
3q29 proximal	6	0.203	0.468	0.664
16p11.2 distal BP1 BP2 BP3	10	0.187	0.387	0.629
2q21.1 BUB1	54	0.171	0.153	0.262
10q22q23 NRG3 GRID1	7	0.127	0.609	0.835
16q23.3	55	0.104	0.116	0.367
22q11.2 distal type III	178	0.081	0.077	0.292
ZMYM5	66	0.063	0.106	0.553
2q13 NPHP1	784	0.043	0.036	0.241
1q21.1 distal TAR	15	0.042	0.304	0.889
15q13.1q13.3 BP3 BP5	214	0.042	0.072	0.558
16p13.11	775	0.037	0.035	0.287
16p12.1	173	0.030	0.078	0.697
1q21.1 TAR	388	0.011	0.051	0.828
15q13.3 BP4.5 BP5 CHRNA7	2660	0.009	0.019	0.630
15q11.2	1849	0.003	0.023	0.884
16p11.2 distal BP2 BP3	105	-0.011	0.095	0.907
1q21.1 distal	148	-0.012	0.081	0.878
22q11.2 distal type I	9	-0.021	0.450	0.962
DMRT1	15	-0.031	0.252	0.901
17q12	95	-0.032	0.100	0.753
16p11.2 proximal BP4 BP5	135	-0.032	0.081	0.695
17p12 HNPP CMT1A	116	-0.039	0.095	0.681
22q11.2 proximal without LCR-A	178	-0.042	0.082	0.612
13q12.12	221	-0.047	0.067	0.487
2q13	68	-0.064	0.118	0.588
ZNF92	202	-0.067	0.065	0.300
15q24	8	-0.081	0.589	0.890
2q11.2	28	-0.083	0.203	0.683
8p23.1	6	-0.083	0.239	0.727
22q11.2 proximal with LCR-A	254	-0.084	0.063	0.182
10q11.21q11.23	38	-0.087	0.170	0.610
15q13.1q13.2 BP3 BP4	20	-0.172	0.293	0.558
7q11.23 distal	22	-0.178	0.225	0.427
4p16.3	9	-0.337	0.330	0.307
17p11.2 Potocki Lupski SMS	5	-0.417	0.406	0.304
7q11.23 WBS	13	-0.628	0.255	0.014

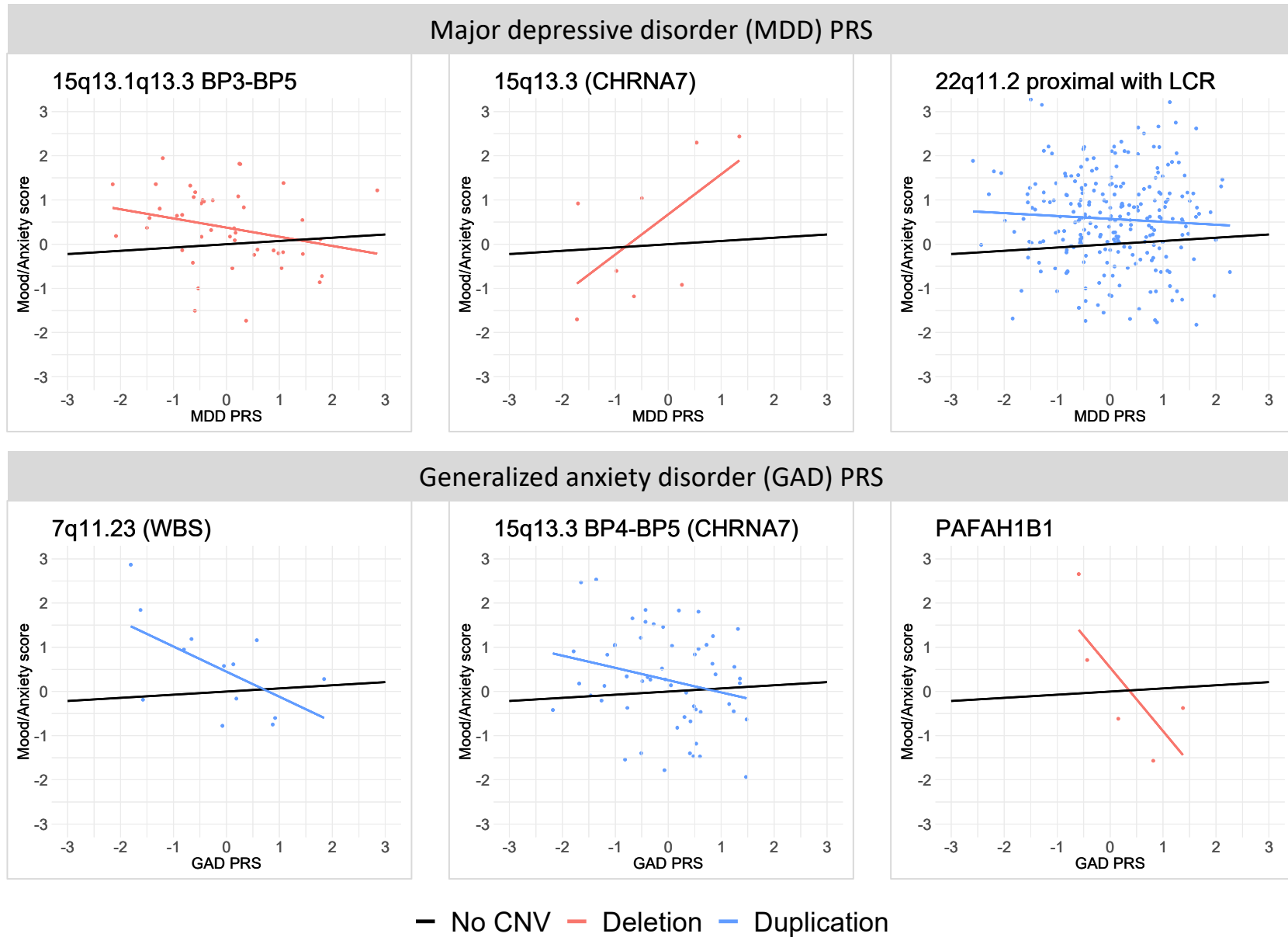
GAD = generalized anxiety disorder; PRS = polygenic risk score.

β coefficients correspond to standardized effect sizes, with values of 0.2, 0.5, and 0.8 indicating small, medium, and large effects, respectively.

Bolded estimates signify nominal significance ($p < 0.05$).

CRS = CNV risk score; LCR = low-copy repeat; BP = breakpoint; TAR = thrombocytopenia-absent radius; WH = Wolf-Hirschhorn; WBS = Williams-Beuren syndrome; PWS/AS = Prader-Willi syndrome / Angelman syndrome; SMS = Smith-Magenis syndrome.

Figure S2 Nominally significant CNV×PRS interactions for individual recurrent CNVs on mood/anxiety factor scores



CNV = copy number variant; PRS = polygenic risk score; MDD = major depressive disorder; GAD = generalized anxiety disorder; BP = breakpoint; LCR = low-copy repeat; WBS = Williams-Beuren syndrome.