

Assortative mating drives pathogenicity of neurodevelopmental disorder-associated variants

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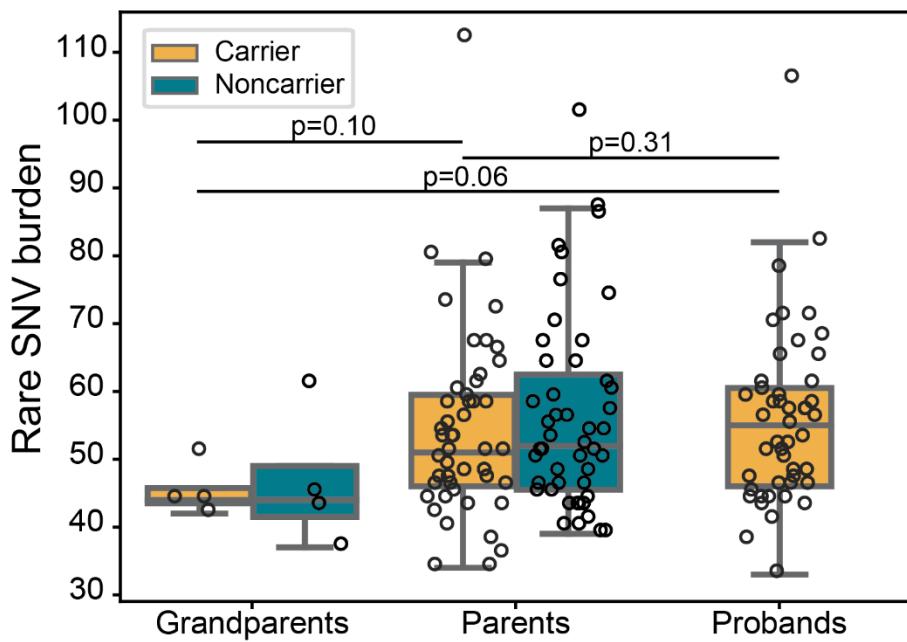


Figure S1. Increases in rare variant burden in 16p12.1 deletion families.

Rare, likely deleterious single nucleotide variant (SNV) burden in carrier and noncarrier grandparents and parents and probands in 16p12.1 deletion families. One tailed t-test, comparisons between carriers in each generation.

SUPPLEMENTAL TABLES

Supplementary Table 1. CNVs in the clinically ascertained CNV cohort.

Region	Number of families	
	Deletion	Duplication
<i>Syndromic</i>		
5q35 (Sotos syndrome region)	1	0
7q11.23 (Williams syndrome region)	15	7
15q11-13 (Prader-Willi syndrome region)	17	0
17q11.2 (Smith-Magenis/Potocki-Lupski)	3	4
17q21.31	3	0
Total Syndromic	39	11
<i>Variably Expressive</i>		
1q21.1	18	26
3q29	6	0
15q11.2	32	0
15q13.3	19	0
16p13.11	20	21
16p11.2	63	35
16p11.2 distal	19	4
16p12.1	8	0
17q12	11	0
22q11.2 (DiGeorge/VCFS region)	25	0
Total Variably Expressive	221	86

Supplementary Table 2. Phenotypes assessed in the Simons Simplex Collection cohort.

Phenotype	Reference
Autism Diagnostic Observation Schedule (ADOS): social affect	1
ADOS: restricted and repetitive behavior domain total score	1
Autism Diagnostic interview (ADI): communication (verbal) domain score	2
ADI: restricted and repetitive behavior domain total score	2
ADI: social domain total score	2
Repetitive Behaviors Scale (RBS)	3
Parent-reported Social Responsiveness Scale (SRS): total raw scores	4
Social Communication Questionnaire (SCQ)	5
Insistence of sameness factor	6
Social interaction factor	6
Sensory-motor behavior factor	6
Self-injurious behavior factor	6
Idiosyncratic repetitive speech and behavior	6
Communication skills factor	6
Vineland Adaptive Behavior Scales: composite standard scores	7
Full-scale IQ	
Verbal IQ	
Nonverbal IQ	
Developmental Coordination Disorders Questionnaire	8
Child Behavior Checklist (CBCL) 2-5 internalizing	9
CBCL 2-5 externalizing	9
CBCL 6-18 internalizing	9
CBCL 6-18 externalizing	9

Supplementary Table 3. Psychiatric phenotype frequencies in SPARK and the UK Biobank.

Disorder	SPARK frequency	UK Biobank frequency
Anxiety	18.35% (2254/12284)	6.40% (2943/45958)
Bipolar Disorder (BPD)	3.54% (435/12284)	0.16% (74/45958)
Depression	21.13% (2596/12284)	8.92% (4099/45958)
Personality Disorder	1.38% (170/12284)	0.06% (29/45958)
Schizophrenia	0.47% (58/12284)	0.03% (12/45958)

SUPPLEMENTAL REFERENCES

1. Lord, C. *et al.* Autism diagnostic observation schedule–2nd edition (ADOS-2). *Los Angel. CA West. Psychol. Corp.* **284**, (2012).
2. Rutter, M., Le Couteur, A., Lord, C., & others. Autism diagnostic interview-revised. *Los Angel. CA West. Psychol. Serv.* **29**, 30 (2003).
3. Bodfish, J. W., Symons, F. J., Parker, D. E. & Lewis, M. H. Repetitive behavior scale—revised. *J. Autism Dev. Disord.* (1999).
4. Constantino, J. N. & Gruber, C. P. *Social responsiveness scale second edition (SRS-2): Manual.* (Western Psychological Services (WPS), 2012).
5. Rutter, M., Bailey, A. & Lord, C. *SCQ: the Social Communication Questionnaire.* (2003).
6. Warrier, V. *et al.* Genetic correlates of phenotypic heterogeneity in autism. *Nat. Genet.* **54**, 1293–1304 (2022).
7. Sparrow, S., Balla, D., Cicchetti, D. & Harrison, P. *Vineland Adaptive Behavior Scales.* (1984).
8. Wilson, B. N. *et al.* Psychometric Properties of the Revised Developmental Coordination Disorder Questionnaire. *Phys. Occup. Ther. Pediatr.* **29**, 182–202 (2009).
9. Achenbach, T. M. The Child Behavior Checklist and related instruments. in *The use of psychological testing for treatment planning and outcomes assessment, 2nd ed.* 429–466 (Lawrence Erlbaum Associates Publishers, 1999).