nature genetics

Article

https://doi.org/10.1038/s41588-024-01710-0

Genetic modifiers of rare variants in monogenic developmental disorder loci

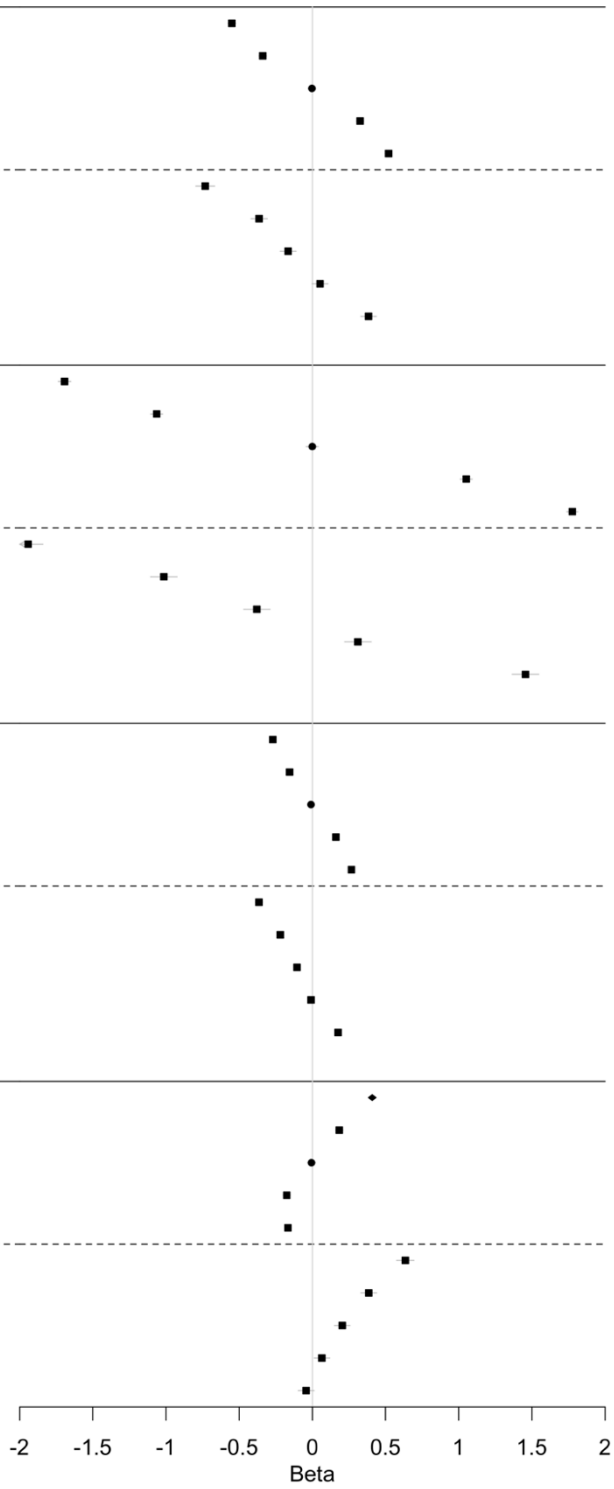
In the format provided by the authors and unedited

SUPPLEMENTARY INFORMATION

Table of contents

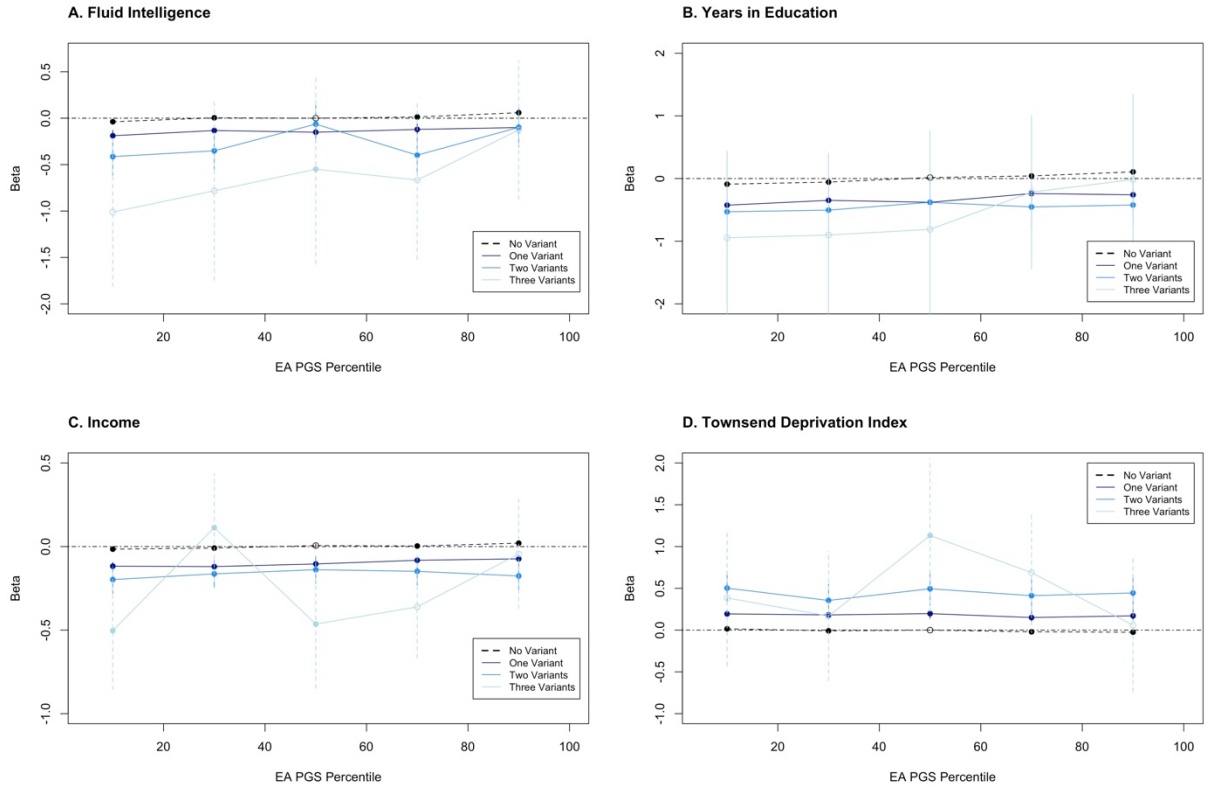
Supplementary Fig. 1: Trait results across EA-PGS quintiles for variant carriers and non-carriers. Data are presented as mean values +/- 95% confidence intervals.

Trait	P Value
Fluid Intelligence	
No Variant Q1	< 1.00E-220
No Variant Q2	2.32E-152
No Variant Q3	0.79
No Variant Q4	3.95E-148
No Variant Q5	< 1.00E-220
Variant Carriers Q1	6.29E-111
Variant Carriers Q2	1.08E-36
Variant Carriers Q3	2.77E-09
Variant Carriers Q4	0.06
Variant Carriers Q5	2.33E-46
Years in Education	
No Variant Q1	< 1.00E-220
No Variant Q2	< 1.00E-220
No Variant Q3	0.96
No Variant Q4	< 1.00E-220
No Variant Q5	< 1.00E-220
Variant Carriers Q1	< 1.00E-220
Variant Carriers Q2	5.57E-106
Variant Carriers Q3	1.86E-16
Variant Carriers Q4	1.74E-11
Variant Carriers Q5	1.95E-218
Income	
No Variant Q1	< 1.00E-220
No Variant Q2	2.15E-205
No Variant Q3	0.05
No Variant Q4	3.45E-226
No Variant Q5	< 1.00E-220
Variant Carriers Q1	3.88E-186
Variant Carriers Q2	1.00E-85
Variant Carriers Q3	2.64E-21
Variant Carriers Q4	0.39
Variant Carriers Q5	2.81E-57
Townsend Deprivation Index	
No Variant Q1	**1.39E-213**
No Variant Q2	1.15E-48
No Variant Q3	0.60
No Variant Q4	7.28E-45
No Variant Q5	3.10E-46
Variant Carriers Q1	1.17E-96
Variant Carriers Q2	1.19E-44
Variant Carriers Q3	6.77E-14
Variant Carriers Q4	0.01
Variant Carriers Q5	0.11

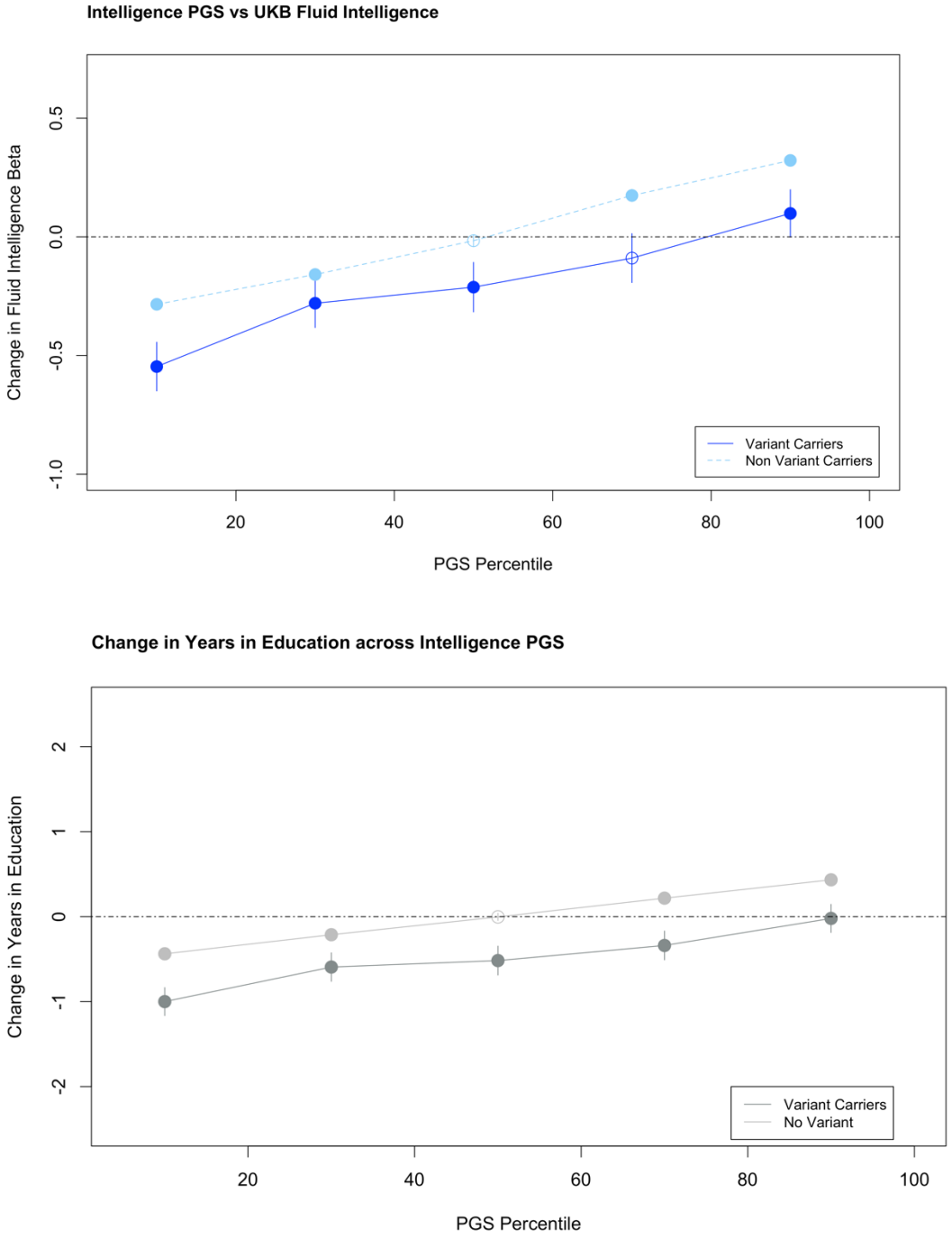


Supplementary Fig. 2: Sensitivity analysis of the additive effect of rare DD variant burden and EA-PGS on DD-related phenotypes.

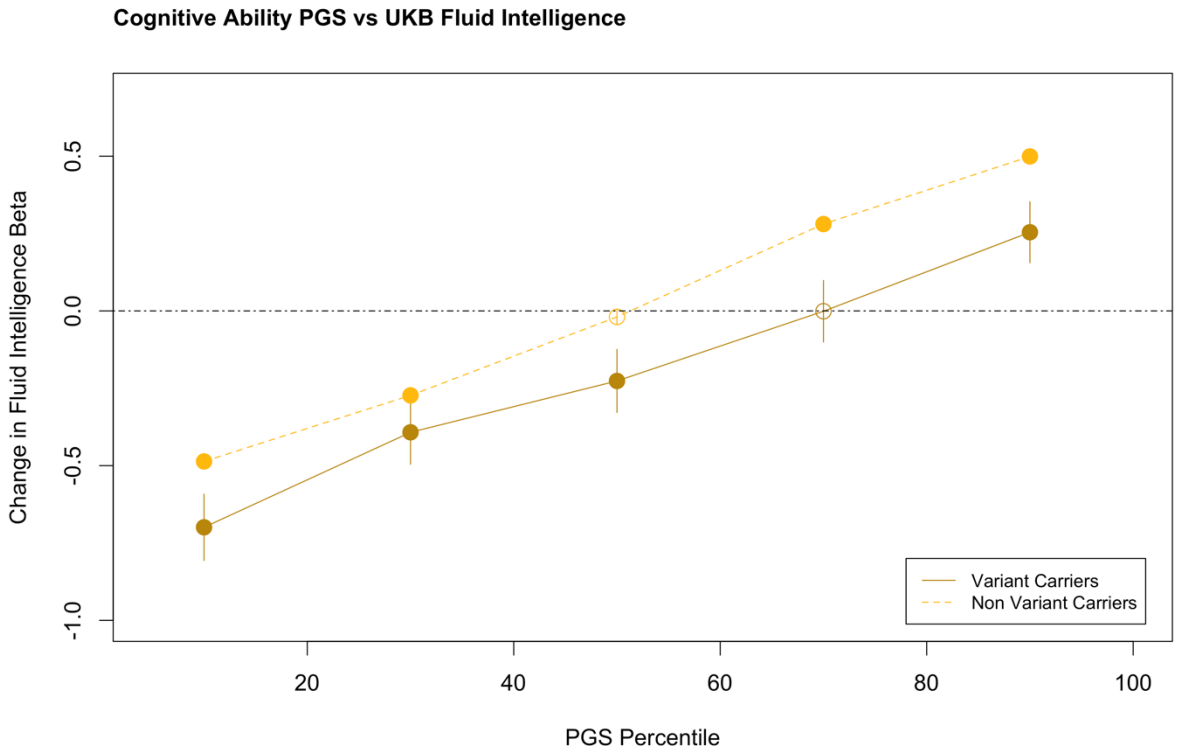
This analysis used 74 SNPs from an EA GWAS that excluded UKB, Okbay *et al.* 2016[1]. Data are presented as mean values +/- 95% confidence intervals.

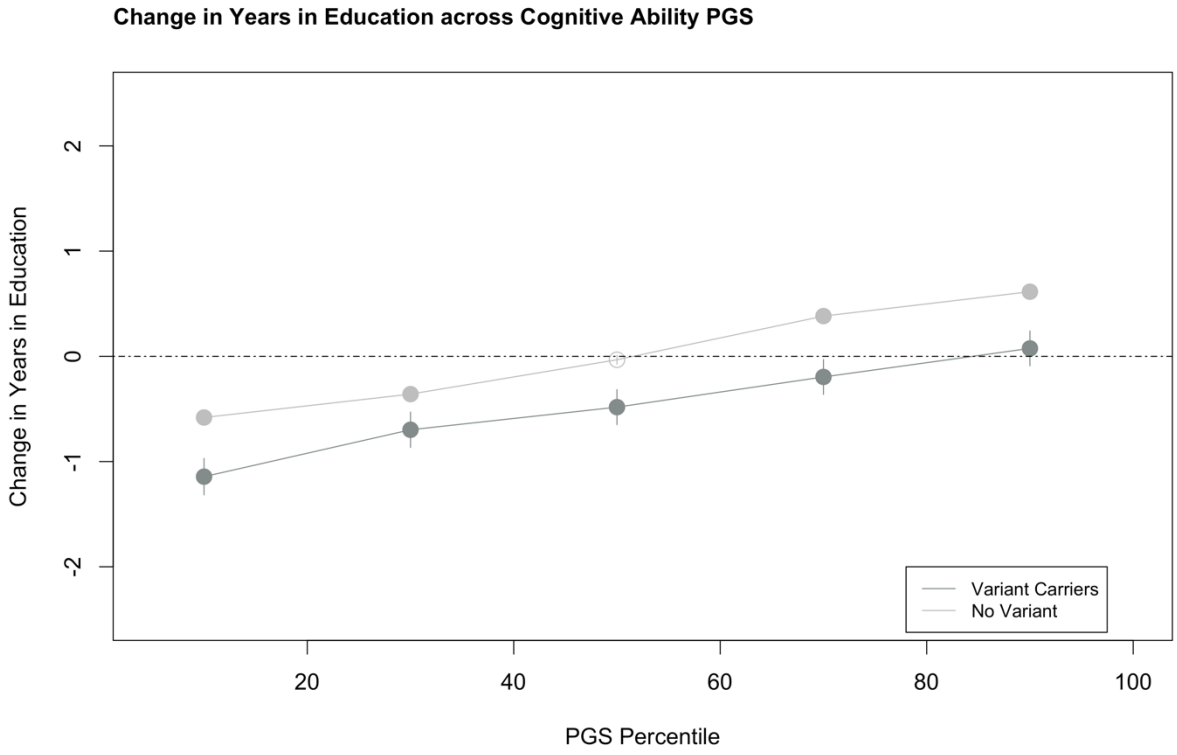


Supplementary Fig. 3: Effect of rare DD variant burden and intelligence PGS on DD-related phenotypes.
Intelligence PGS is derived from Savage *et al.* 2018[2] and Data are presented as mean values +/- 95% confidence intervals.

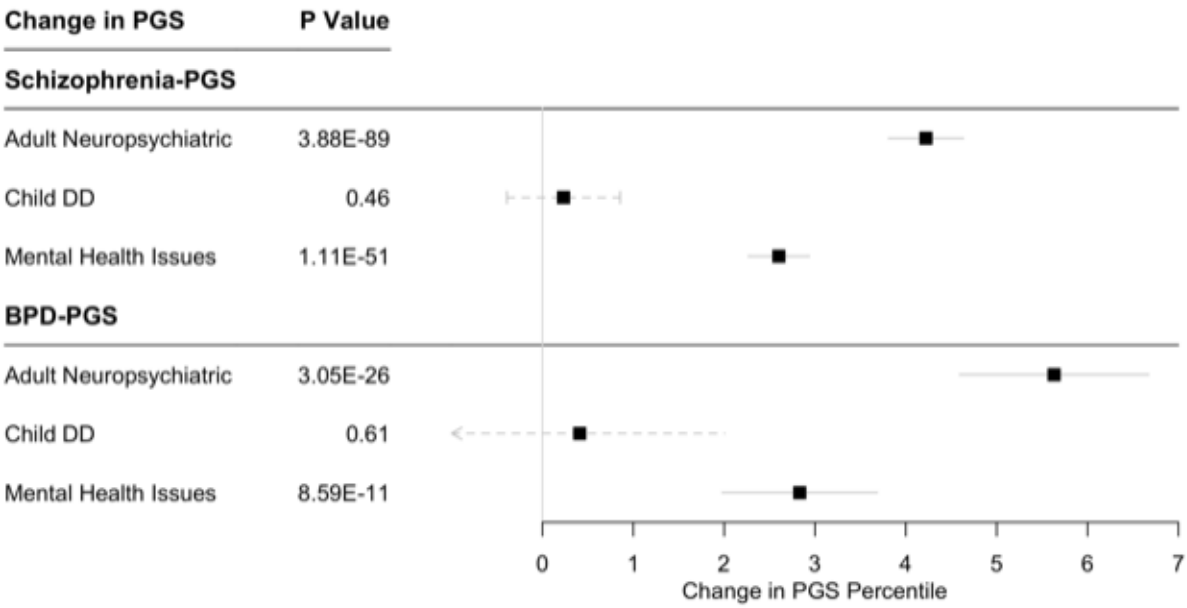


Supplementary Fig. 4: Effect of rare DD variant burden and cognitive ability PGS on DD-related phenotypes.
Cognitive ability PGS is derived Genç *et al* 2021[3]. Data are presented as mean values +/- 95% confidence intervals.





Supplementary Fig. 5: Average change in schizophrenia PGS and bipolar disorder PGS among rare DD variant carriers with a relevant clinical diagnosis.
Data are presented as mean values +/- 95% confidence intervals.



Supplementary References

1. Okbay, A. *et al.* Genome-wide association study identifies 74 loci associated with educational attainment. *Nature* **533**, 539–542 (2016).
2. Savage, J. E. *et al.* Genome-wide association meta-analysis in 269,867 individuals identifies new genetic and functional links to intelligence. *Nat. Genet.* **50**, 912–919 (2018)
3. Genç, E. *et al.* Polygenic Scores for Cognitive Abilities and Their Association with Different Aspects of General Intelligence—A Deep Phenotyping Approach. *Mol. Neurobiol.* **58**, 4145–4156 (2021).