



Variants impacting language in autism also influence the general population

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We have nothing to disclose

DSM-5 diagnostic criteria

Autism spectrum disorder (ASD)

1. Deficits in social communication
2. Restrictive and/or repetitive behavior

Schizophrenia

1. Delusions
2. Hallucinations
3. Disorganized speech
4. Negative symptoms

Language problems

Bipolar I Disorder


1. Manic episode
 - a. Grandiosity
 - b. Decreased need for sleep
 - c. More talkative than usual

Tourette's Disorder

1. Multiple motor and vocal tics
2. Tics persisted for at least 1 year
3. Onset before 18 years old

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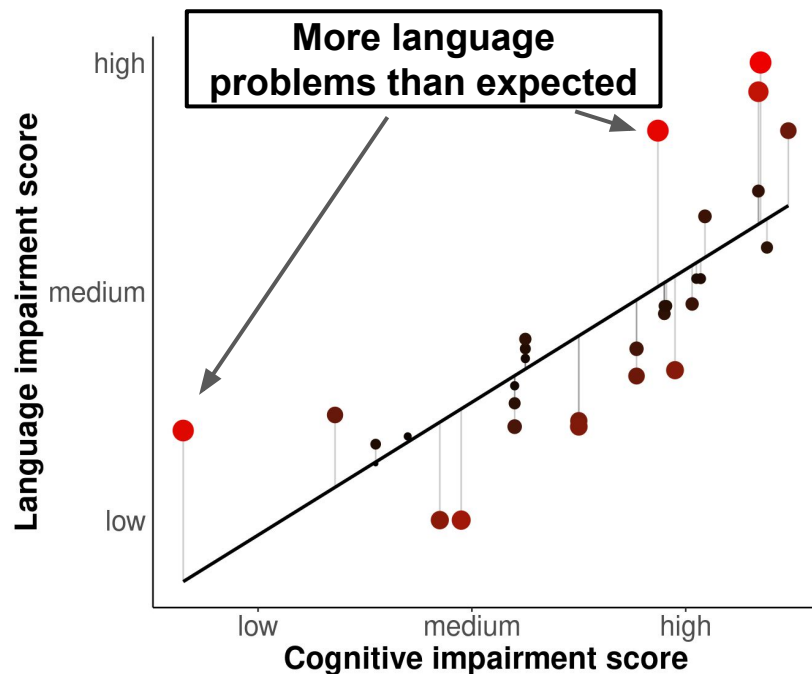
Are language problems being driven by
autism genetic risk factors?

Phenotypes:

- **Language level for their age**
- Cognitive level for their age

*Specific language impairment** (SLI) score

- Residualized for:
 - Age & assigned sex
 - Cognitive impairment, deafness
 - CNVs / de novo variants
 - 20 genetic PCs

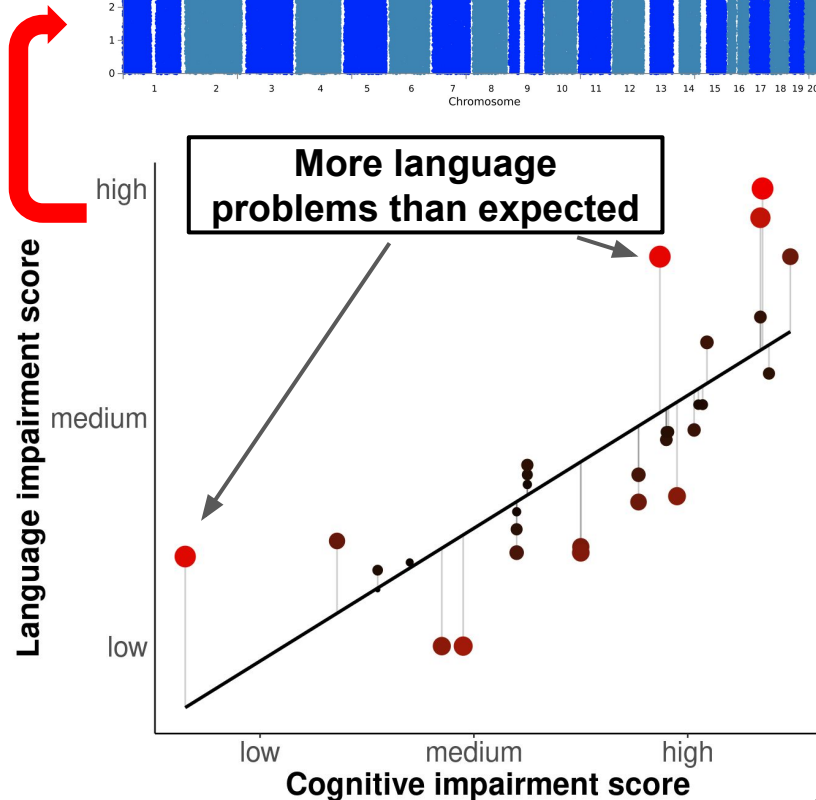
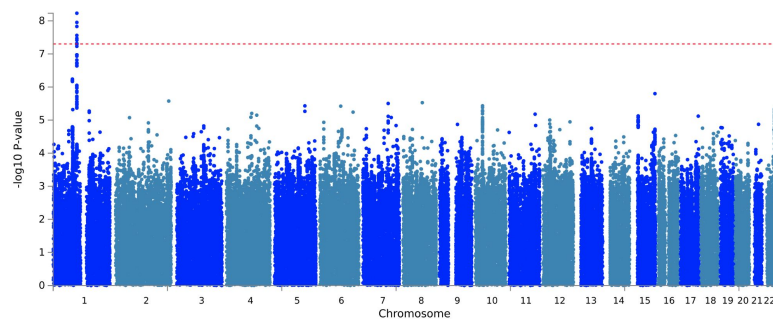


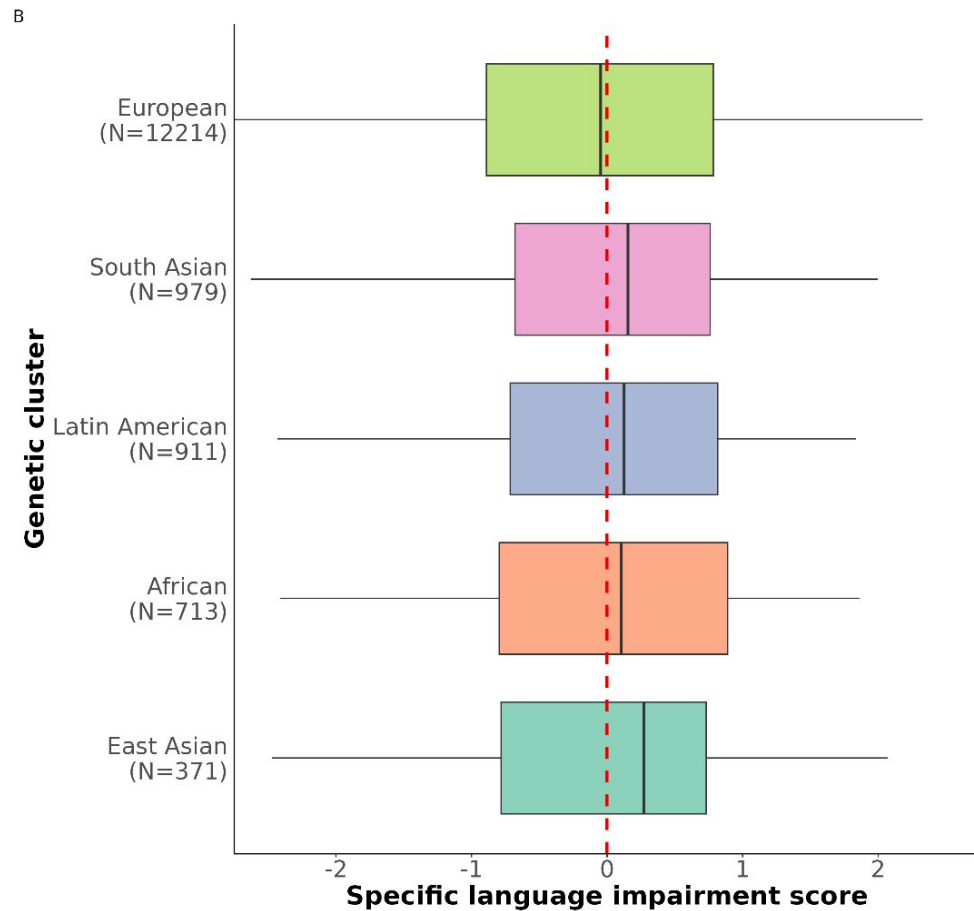
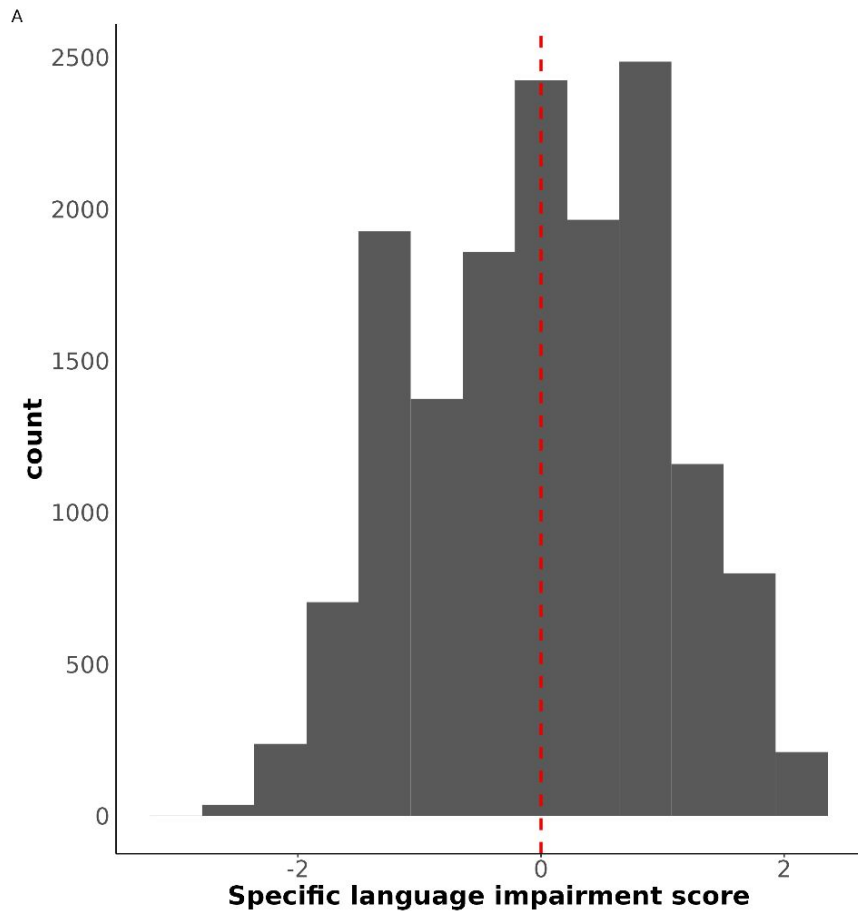
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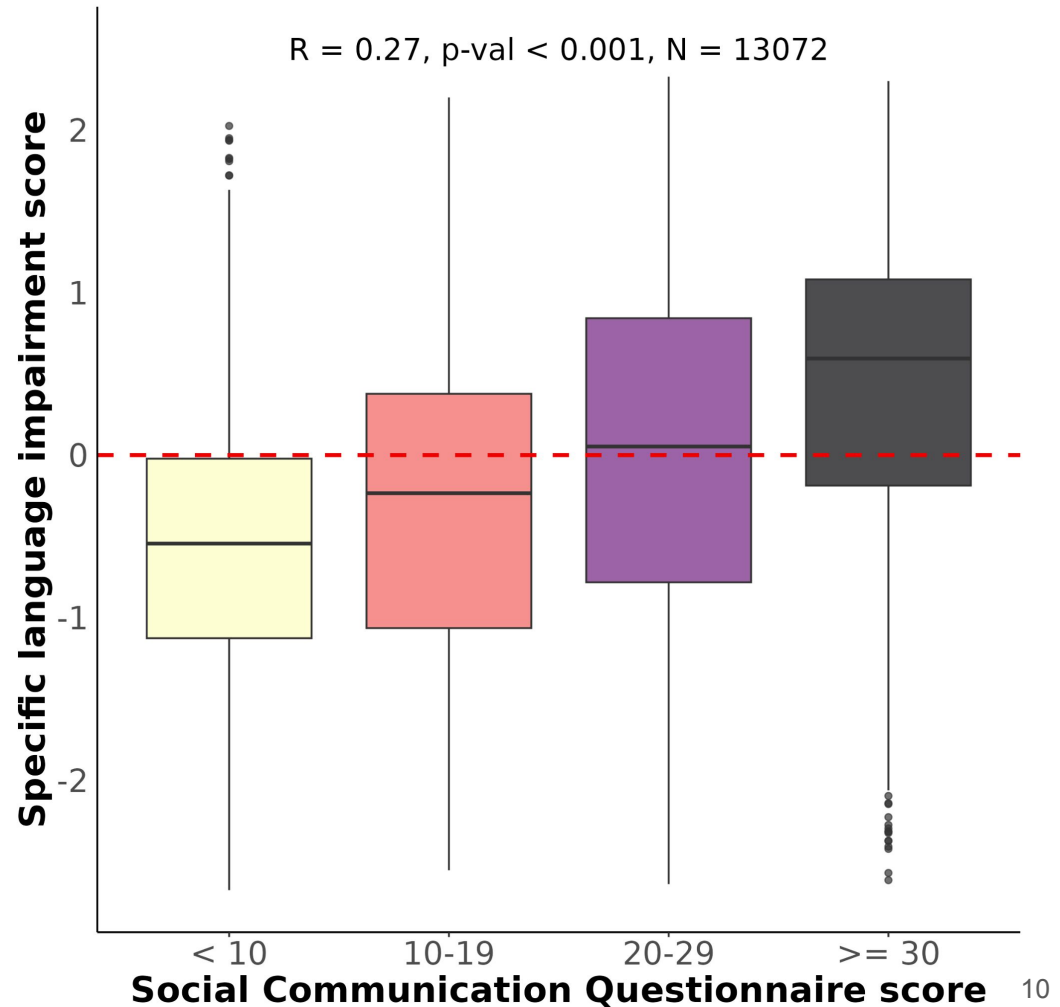
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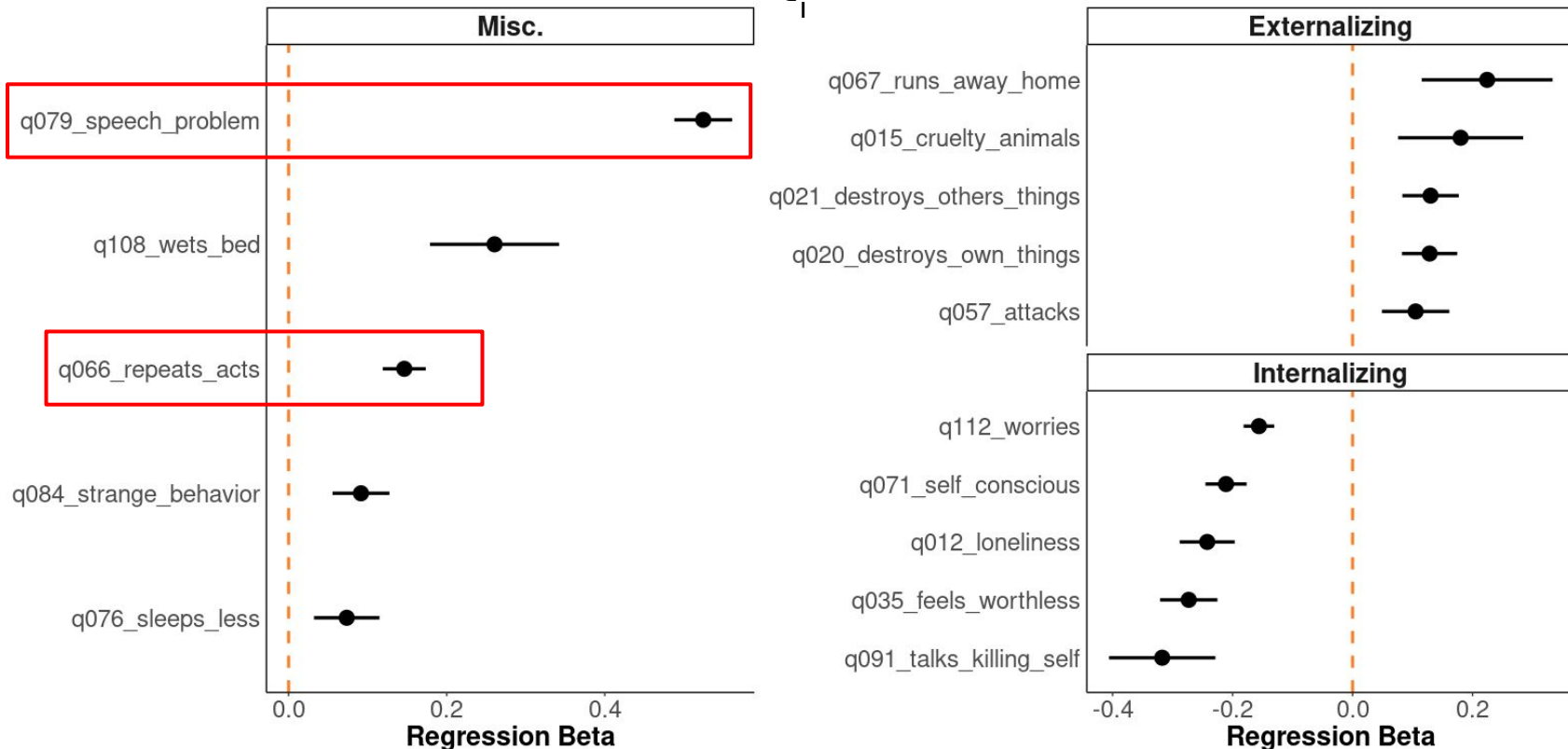
SLI scores are associated with
core autism phenotypes

**Language problems
are associated with
ASD social problems**



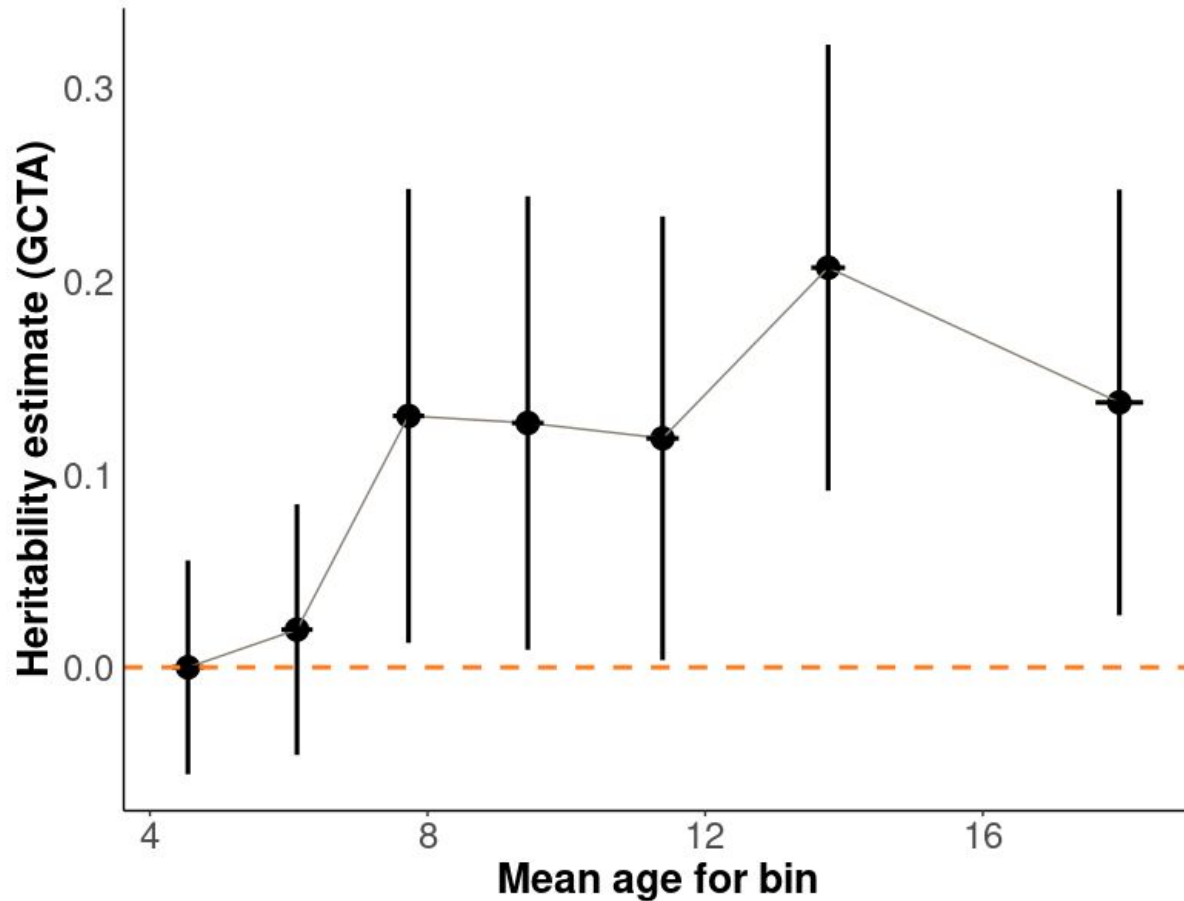
SLI scores are associated with externalizing behaviors

$$CBCL\ Score_i \sim Intercept + \beta_1 SLI\ Score_i + \beta_2 Age_i + \beta_2 Sex_i + \epsilon_i$$

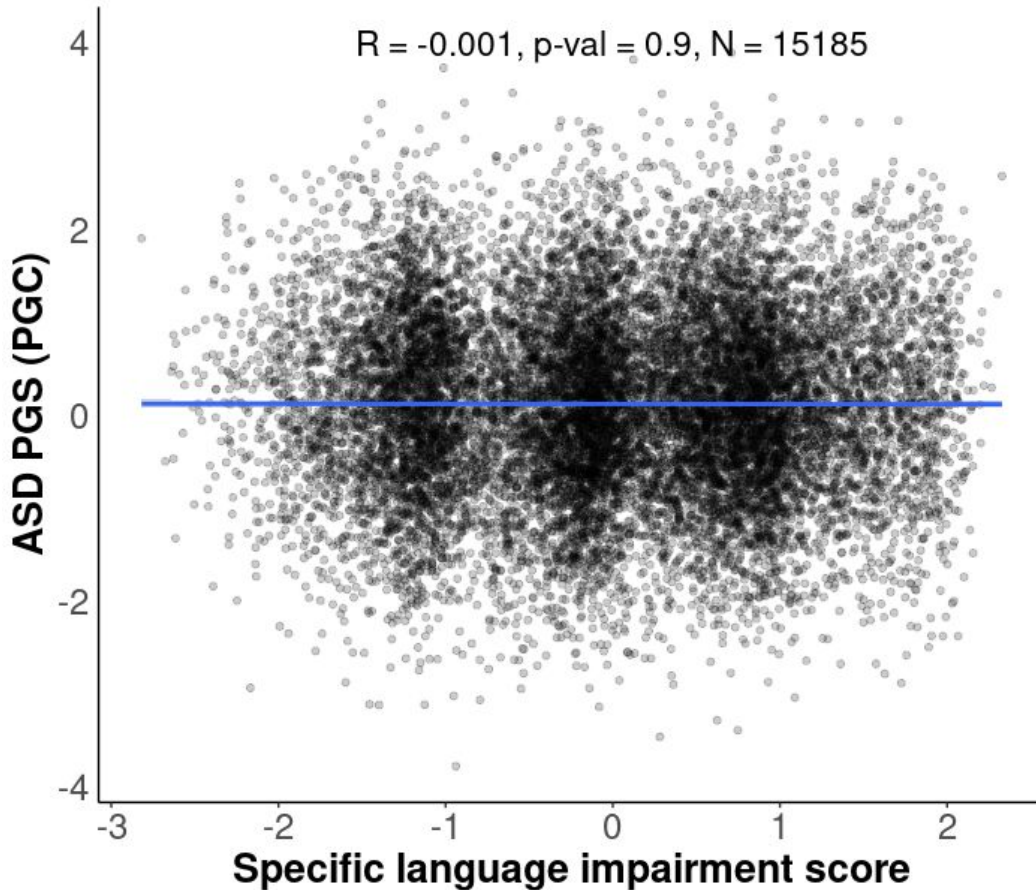


Genetic analysis

Heritability estimates vary with age



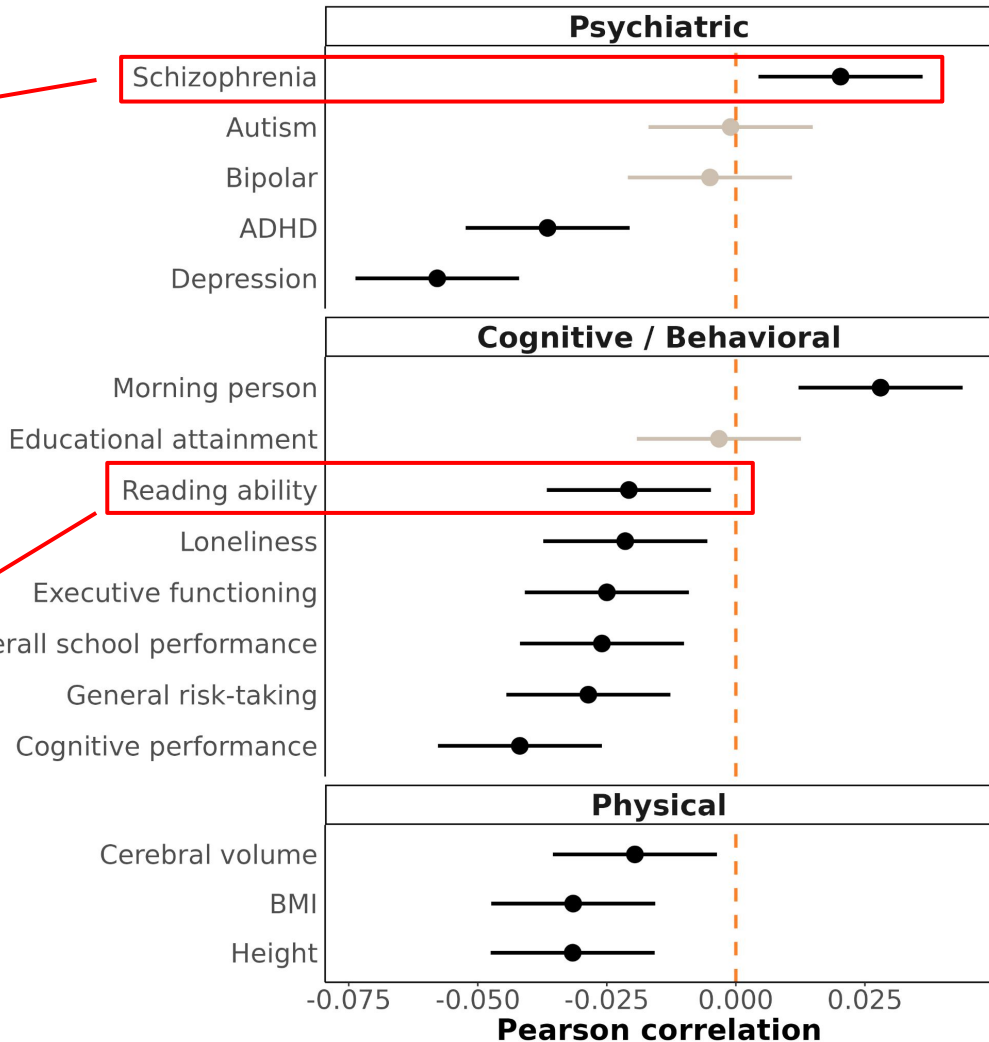
Autism PGS is not associated with language problems

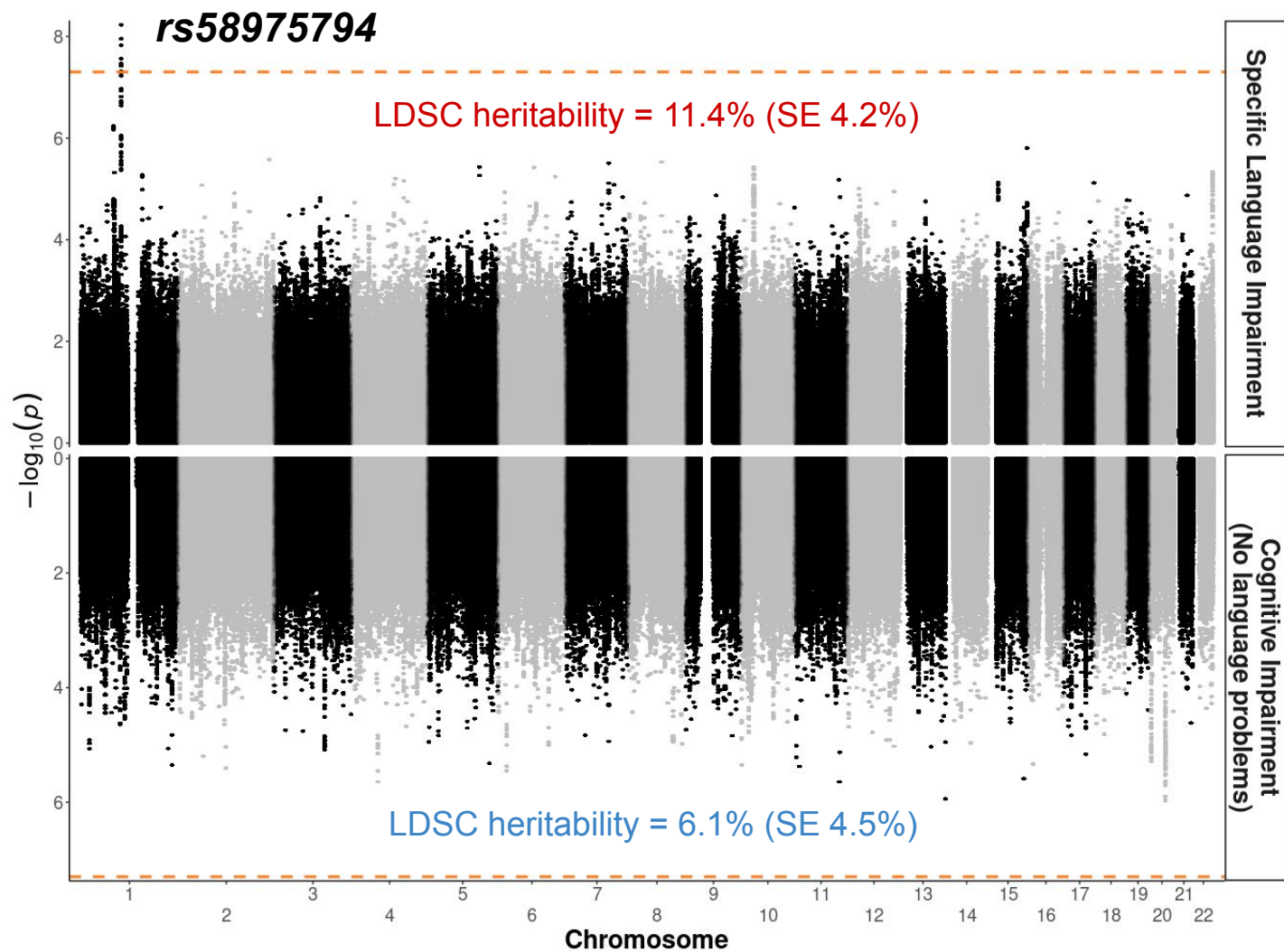


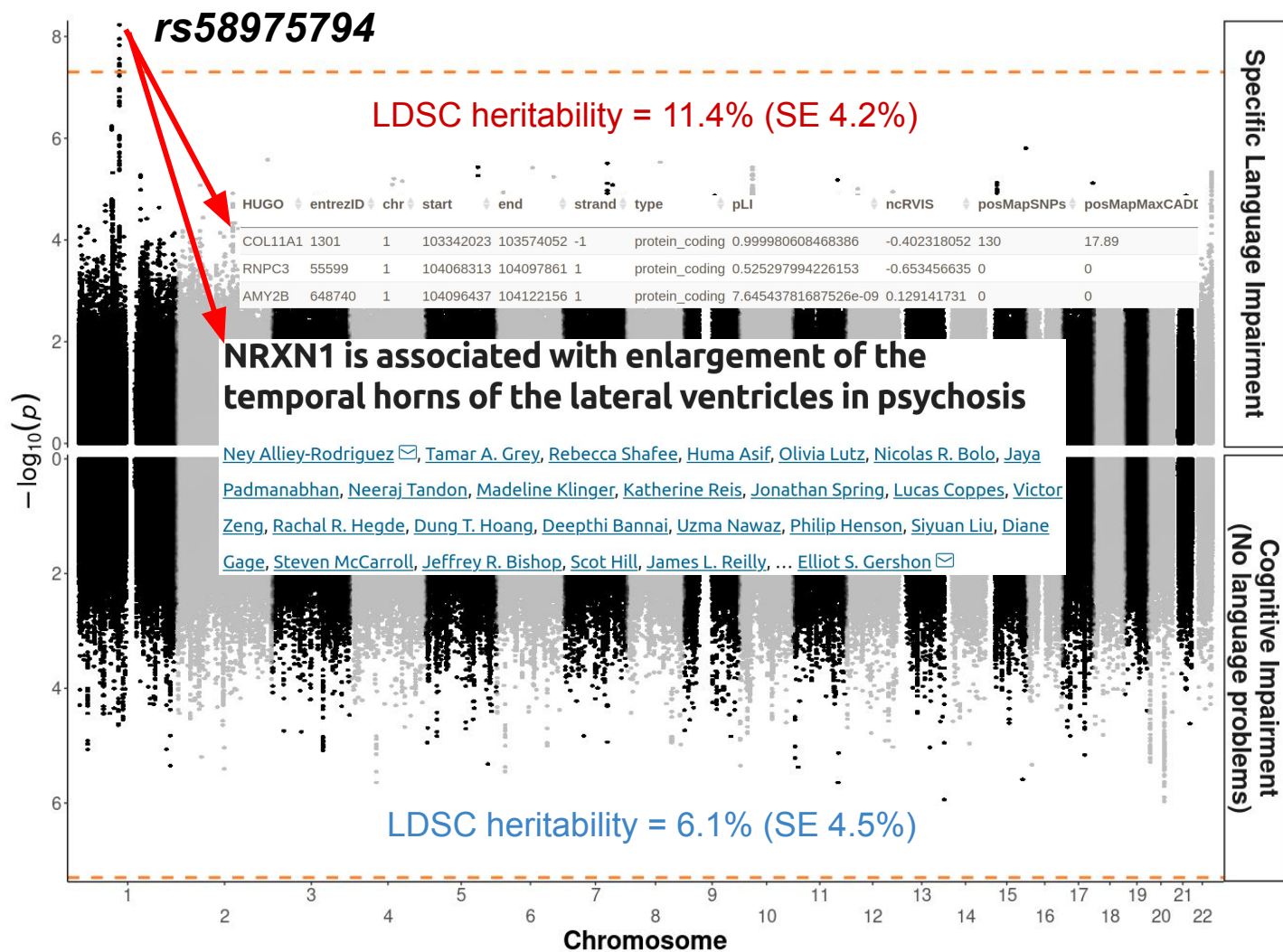
↑ SLI = ↑ schizophrenia PGS

Polygenic scores

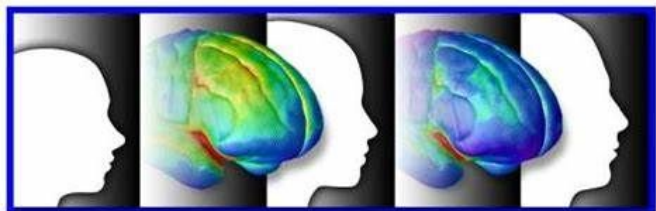
↑ SLI = ↓ reading ability PGS







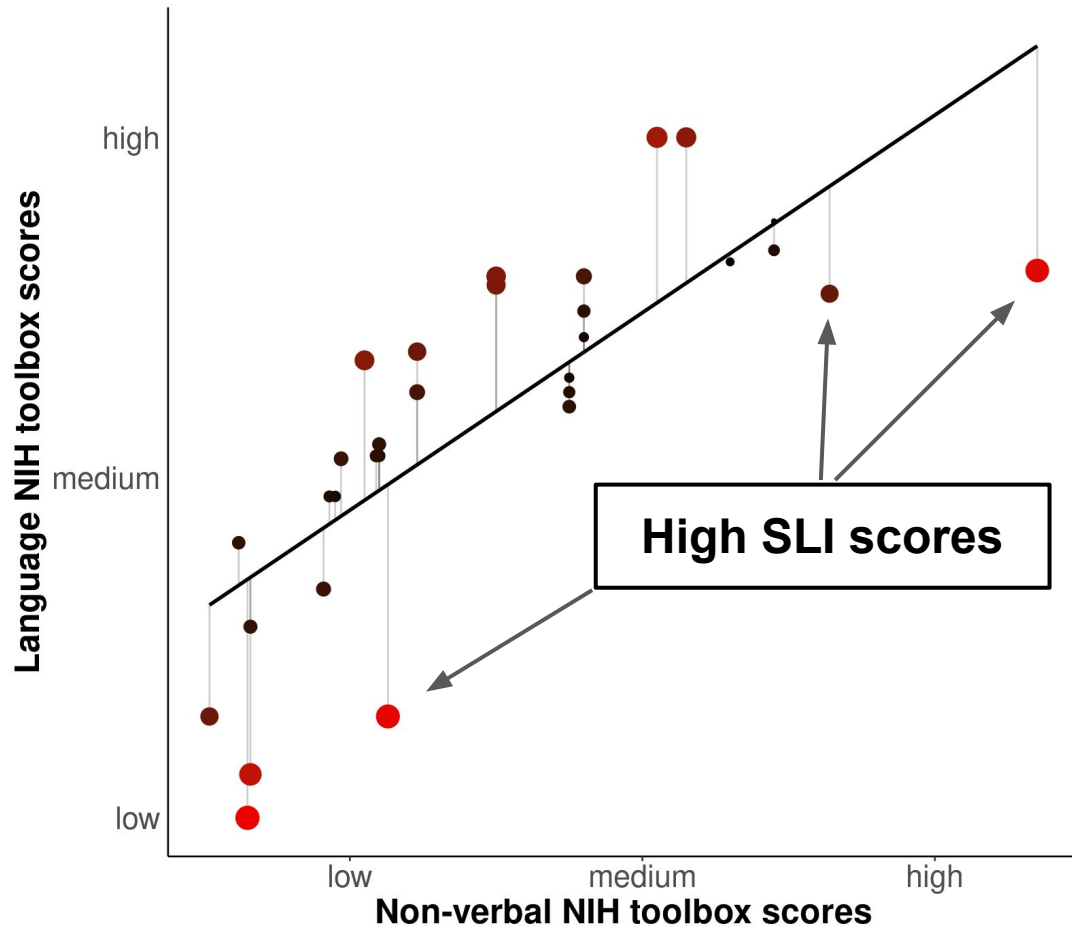
SLI associated variants discovered in ASD
translate to the general population



Adolescent Brain Cognitive Development

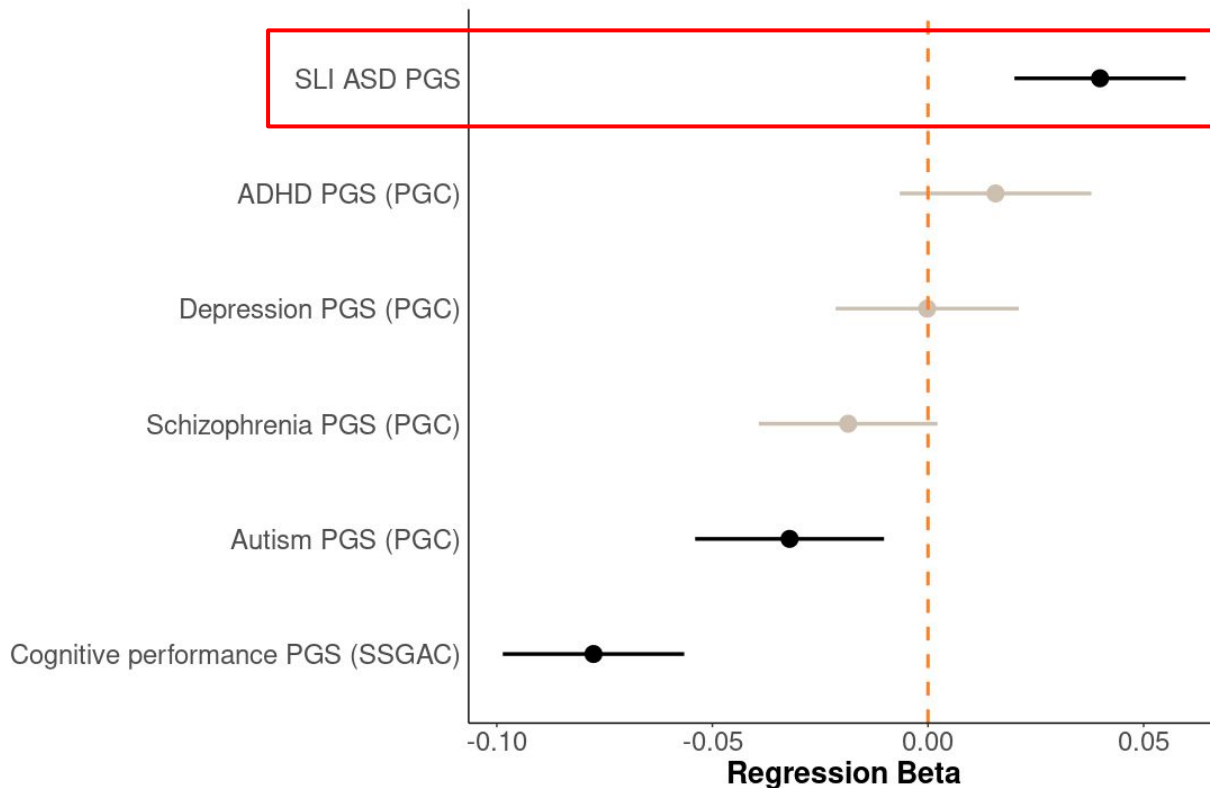


N = 9,723



SLI variants from autism are generalizable

$$SLI\ Score_i \sim Intercept + \beta_1 PGS_{SLI\ i} + \beta_2 PGS_{ADHD\ i} + \dots + \epsilon_i$$

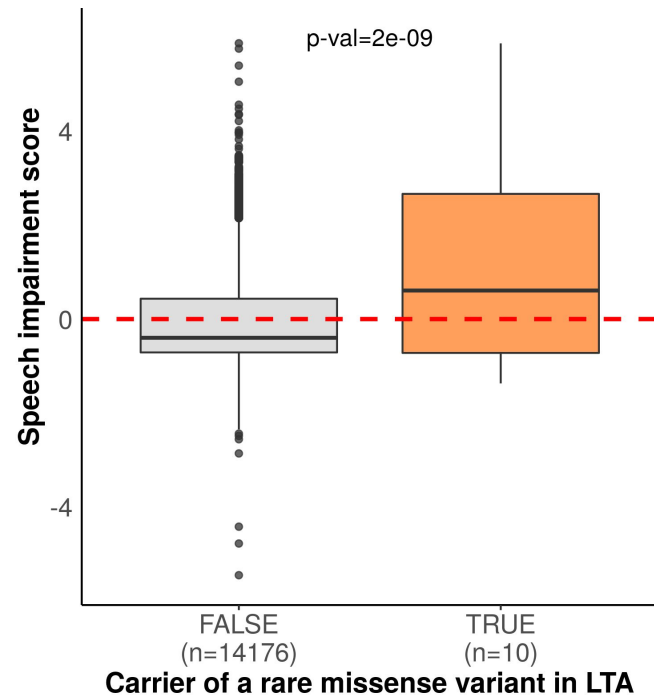
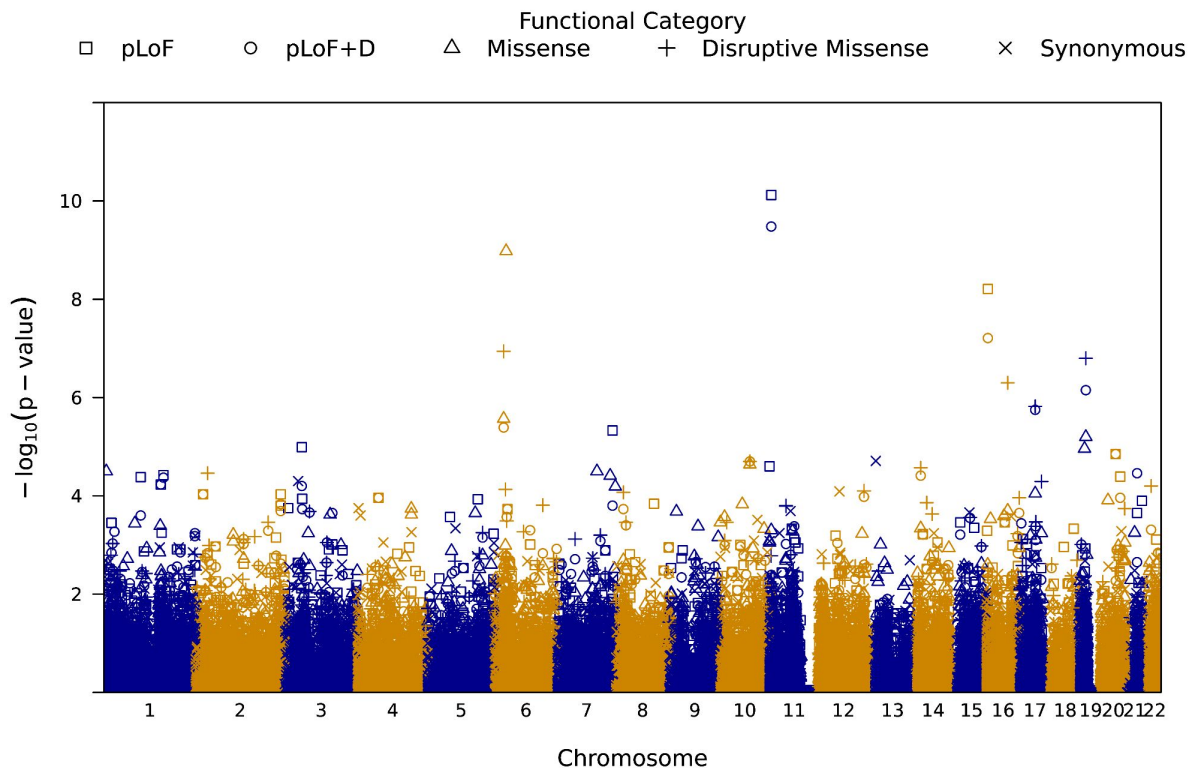


Conclusions and future directions

Conclusions

- Language impairments are associated with autism **phenotypes**
 - **Not** associated with **autism polygenic risk**
- Heritability **changes with age** in language phenotypes
- Genetic studies of traits in ASD-only samples **are generalizable** to the general population

Future directions



Data + tools

Software:

- PLINK, GCTA, fastGWA, KING, LDSC, FUMA, LDPre2
- R, Python

Data:

- SPARK
- ABCD
- GWAS summary statistics from the PGC, SSGAC, and gwas catalog

Acknowledgements

Michaelson Lab @ Ulowa

- **Jacob Michaelson**
- Ethan Bahl
- Muhammad Elsadany
- Annie Gleason
- Grace Kim
- Camilla Strathearn

SPARK

ABCD

PGC

WCPG

IOWA

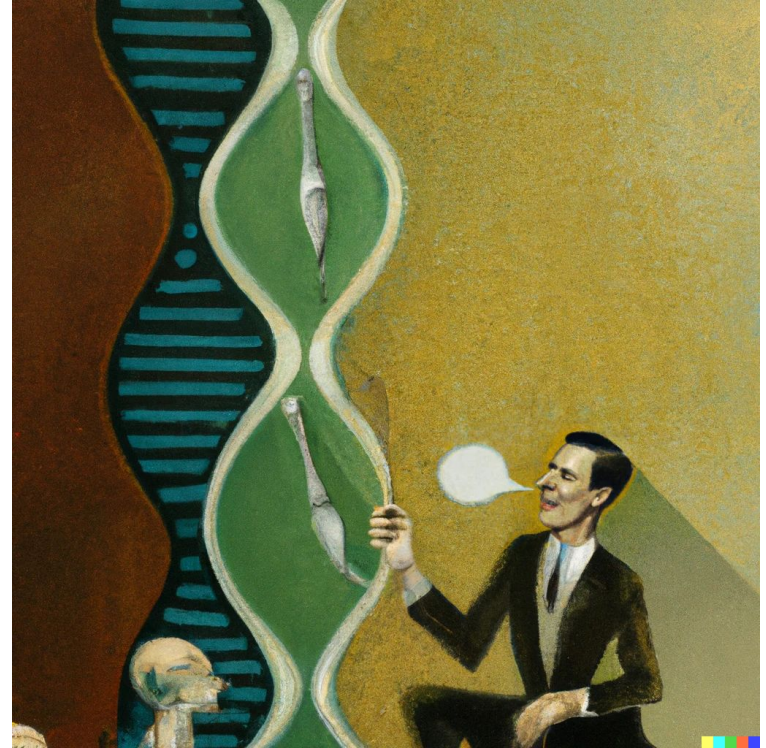


Interdisciplinary
Graduate Program
in Genetics

Questions?

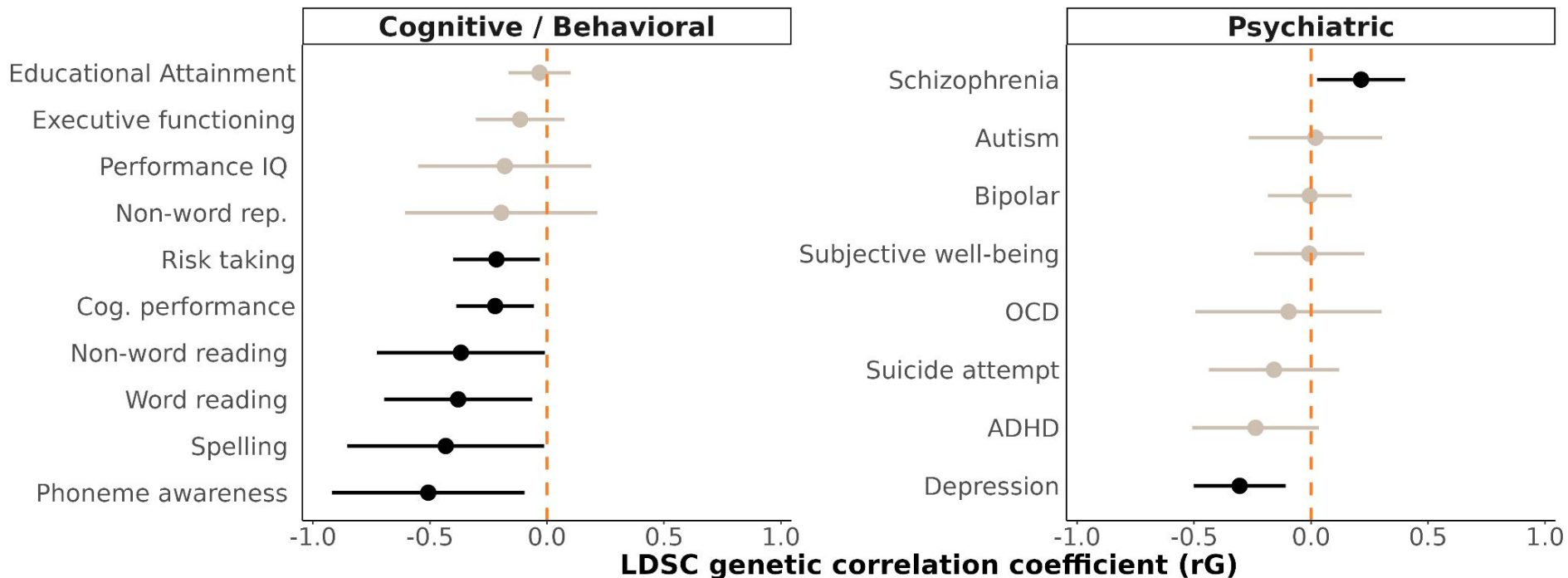
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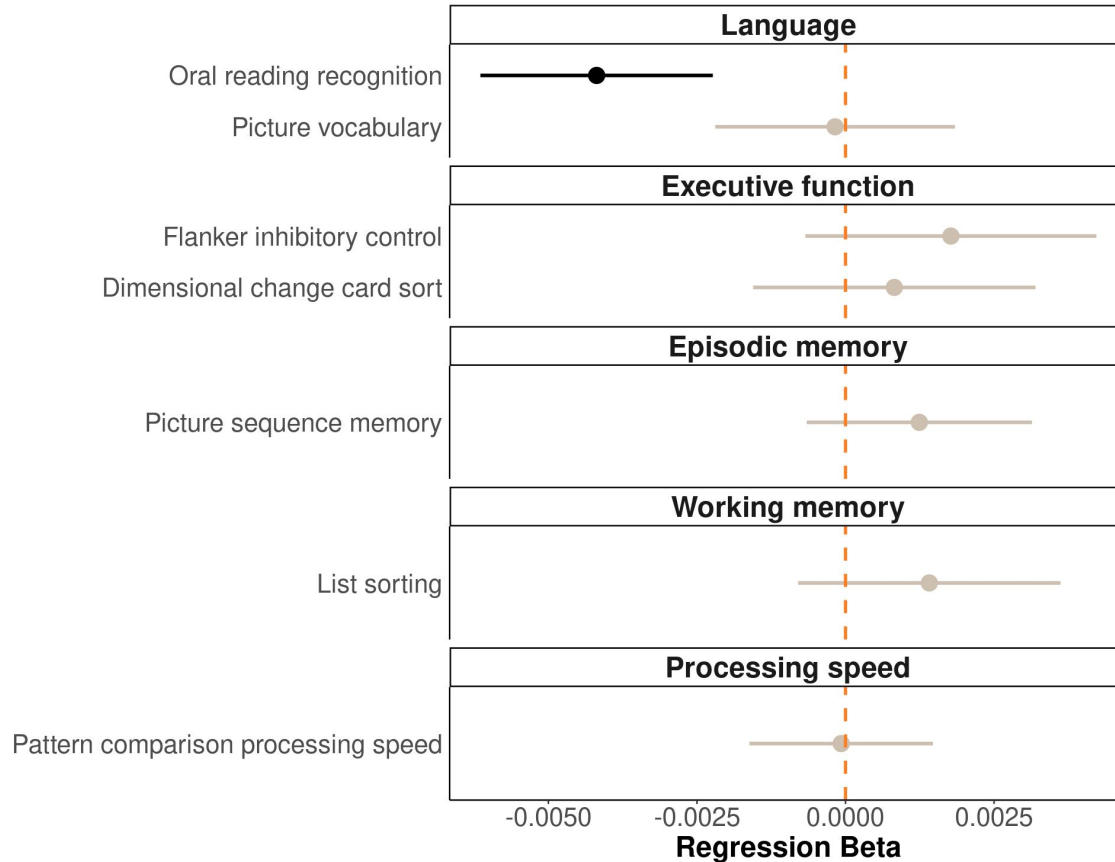


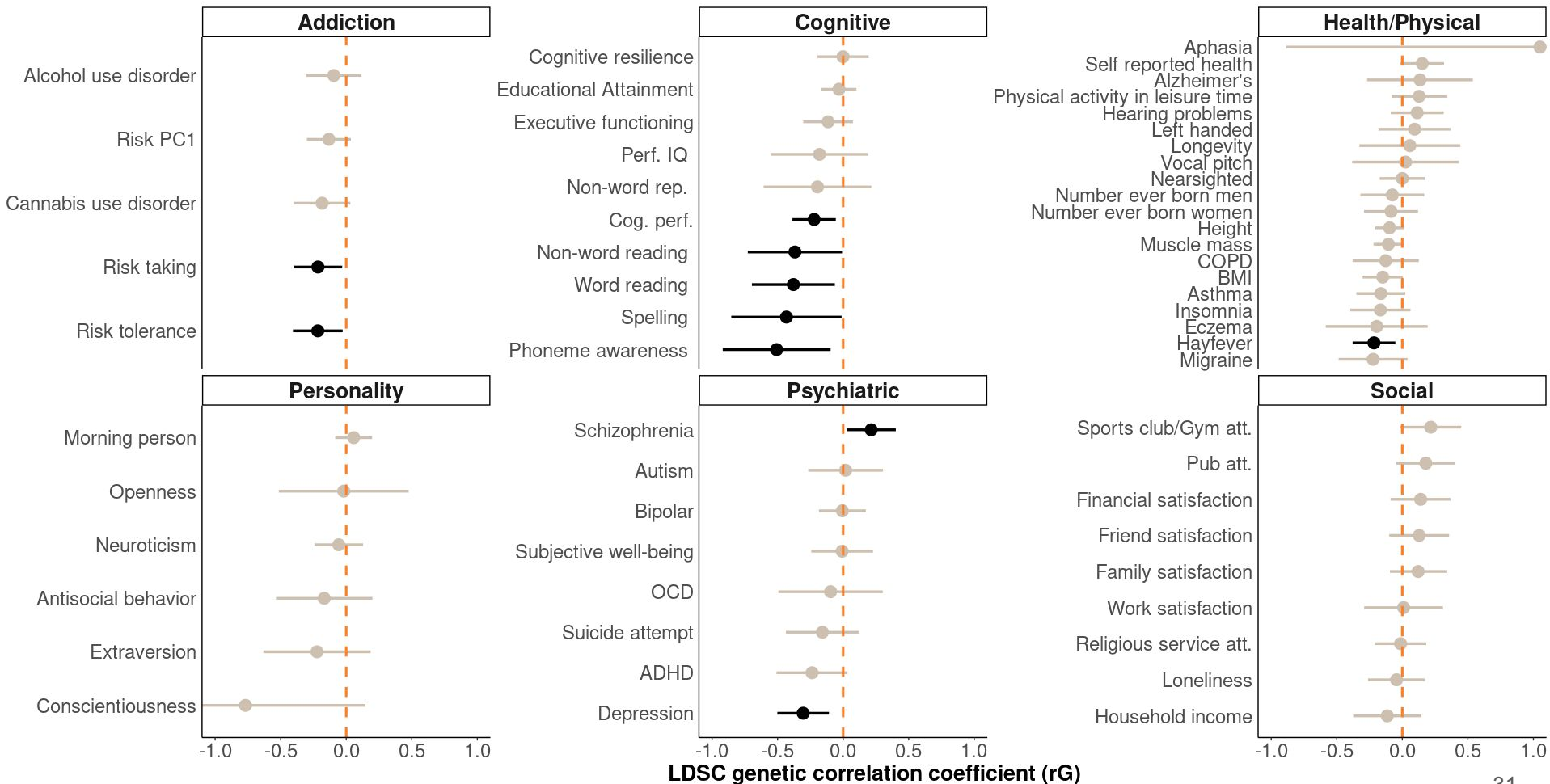
Extra slides

Shared genetic architectures



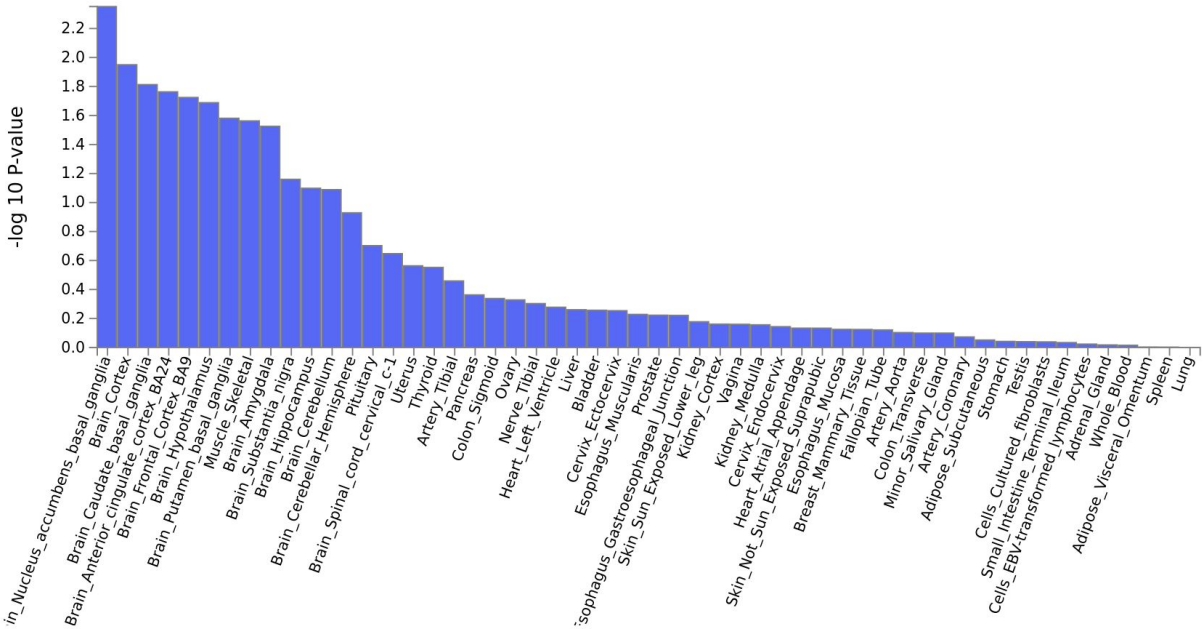
SLI variants from autism impact reading





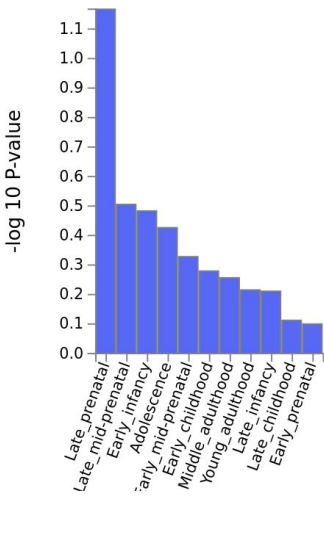
GTEx v8 53 tissue types








Download the plot as [PNG](#) [JPG](#) [SVG](#) [PDF](#)



BrainSpan 11 general developmental stages of brain samples

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Gene Set	 N genes	 Beta	 Beta STD	 SE	 P	 P _{bon}	
GOBP_REGULATION_OF_PROTEIN_LIPIDATION	11	0.91001	0.021875	0.22257	2.1794e-05	0.370694146	
GOCC_PROTEASOME_REGULATORY_PARTICLE_BASE_SUBCOMPLEX	9	0.87806	0.019093	0.22889	6.2724e-05	1	
GOBP_PROTEIN_CATABOLIC_PROCESS_IN_THE_VACUOLE	21	0.58601	0.019459	0.15564	8.3497e-05	1	
GOBP_REGULATION_OF_LIPOPROTEIN_METABOLIC_PROCESS	18	0.70184	0.021578	0.18846	9.8303e-05	1	
GOCC_CALCIUM_AND_CALMODULIN_DEPENDENT_PROTEIN_KINASE_COMPLEX	5	1.3675	0.022167	0.36823	0.00010239	1	
GOBP_NATURAL_KILLER_CELL_CHEMOTAXIS	6	1.3165	0.023376	0.36674	0.00016599	1	
GOMF_FATTY_ACID_OMEGA_HYDROXYLASE_ACTIVITY	8	0.9262	0.018989	0.25868	0.00017194	1	
GOBP_REGULATION_OF_OSTEOBLAST_DIFFERENTIATION	121	0.26788	0.021296	0.075753	0.00020347	1	
GOBP_REGULATION_OF_NATURAL_KILLER_CELL_CHEMOTAXIS	4	1.6128	0.023383	0.45759	0.00021271	1	
GOBP_REGULATION_OF_NEURONAL_SYNAPTIC_PLASTICITY	55	0.40277	0.021624	0.11511	0.00023416	1	

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social problems**

