

# Childhood and adolescent internalising problems: GWAS of ~250k observations points to heterogeneous genetic architecture

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## INTRODUCTION

- Early symptoms of anxiety & depression are associated with the development of mood disorders in later life
- Little is known about the genetic architecture of childhood and adolescent internalising problems

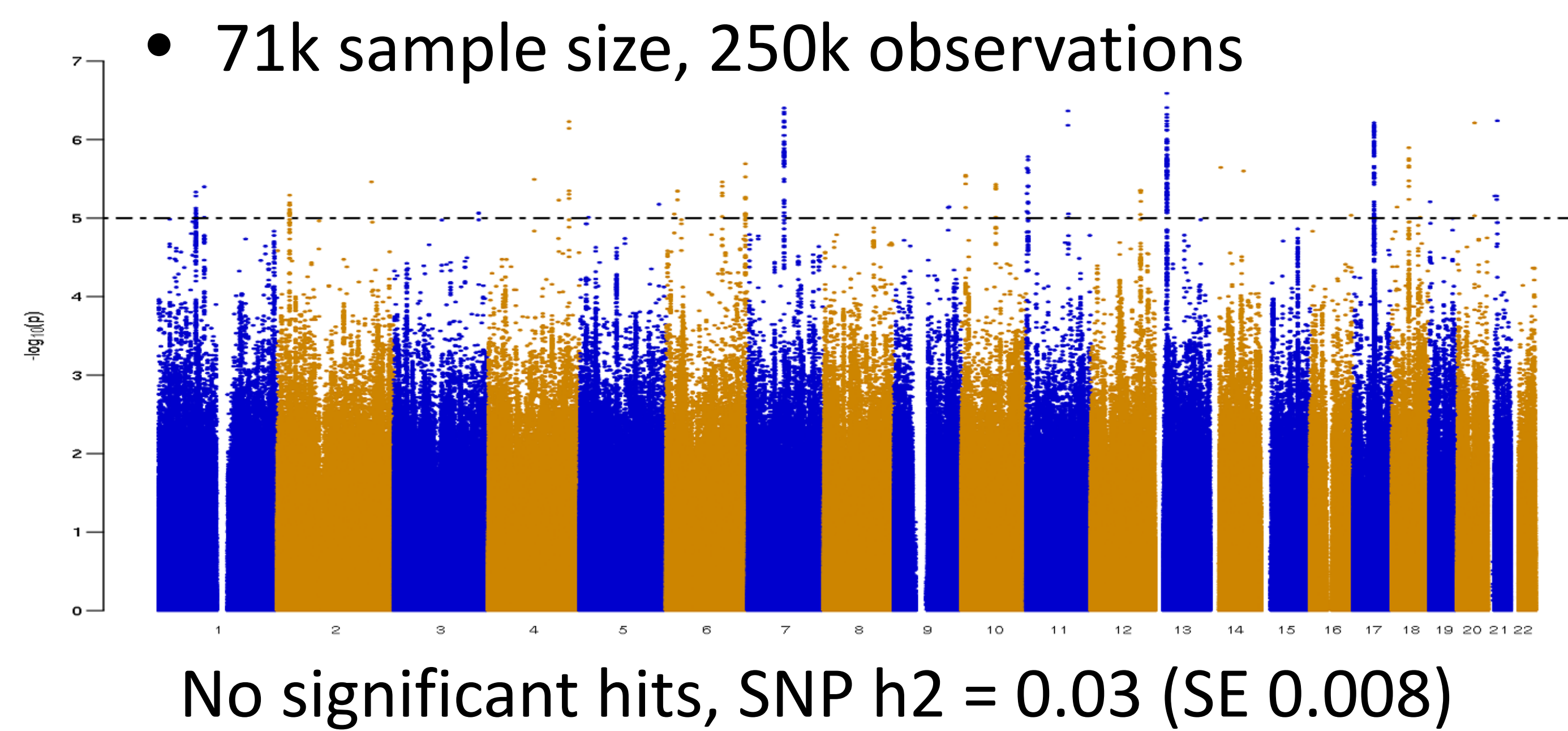
## METHODS

125 univariate GWASes in 22 cohorts of European ancestry, across Europe, Australia, and the US

- Repeated measurements between ages 3 – 18
- 5 raters (mother, father, self, teacher, co-twin)
- 11 measures (most common: CBCL & SDQ)

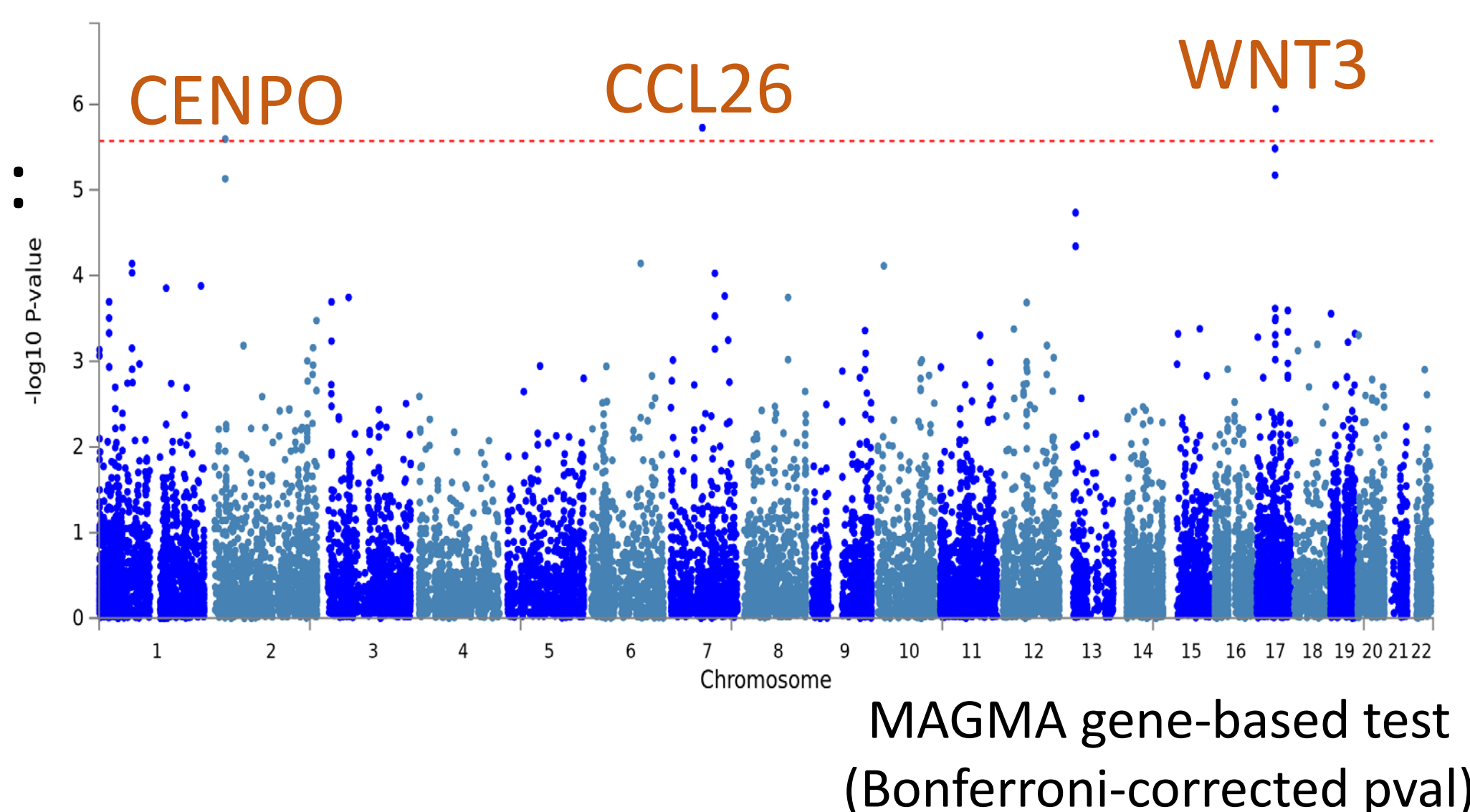
N-weighted meta-analysis to adjust for sample overlap due to repeated measurements

## PRELIMINARY RESULTS



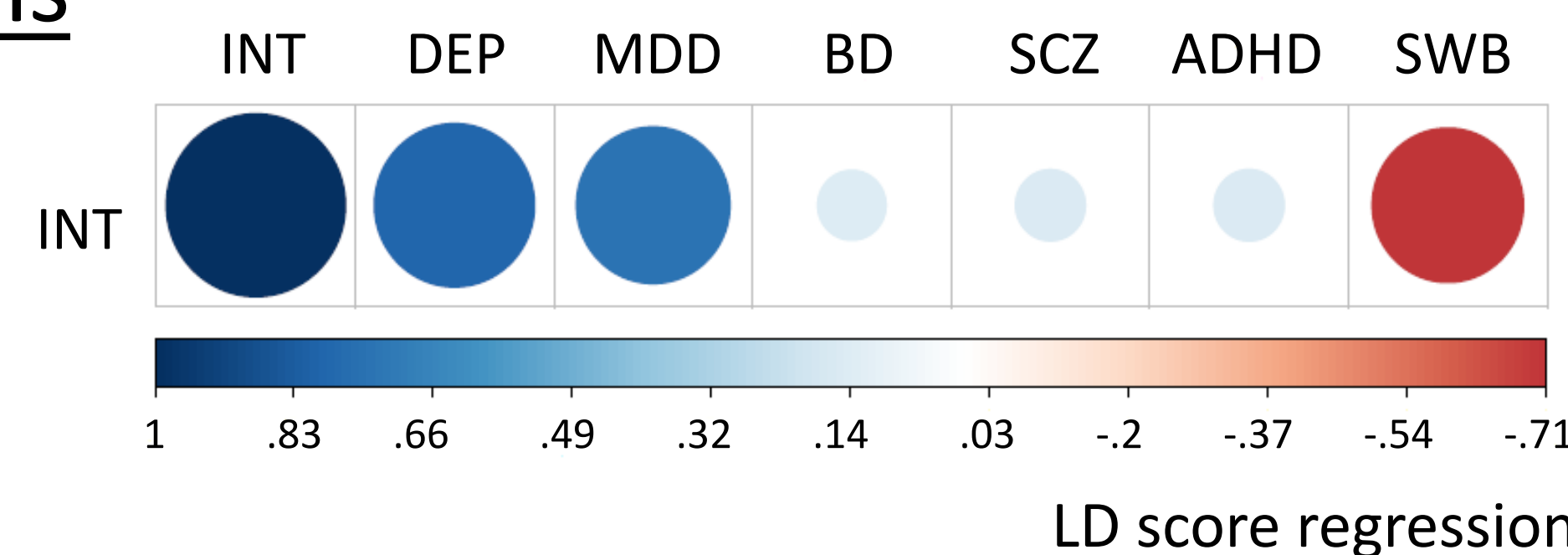
### Genes

3 genes identified:  
prior associations with depression & antidepressant response



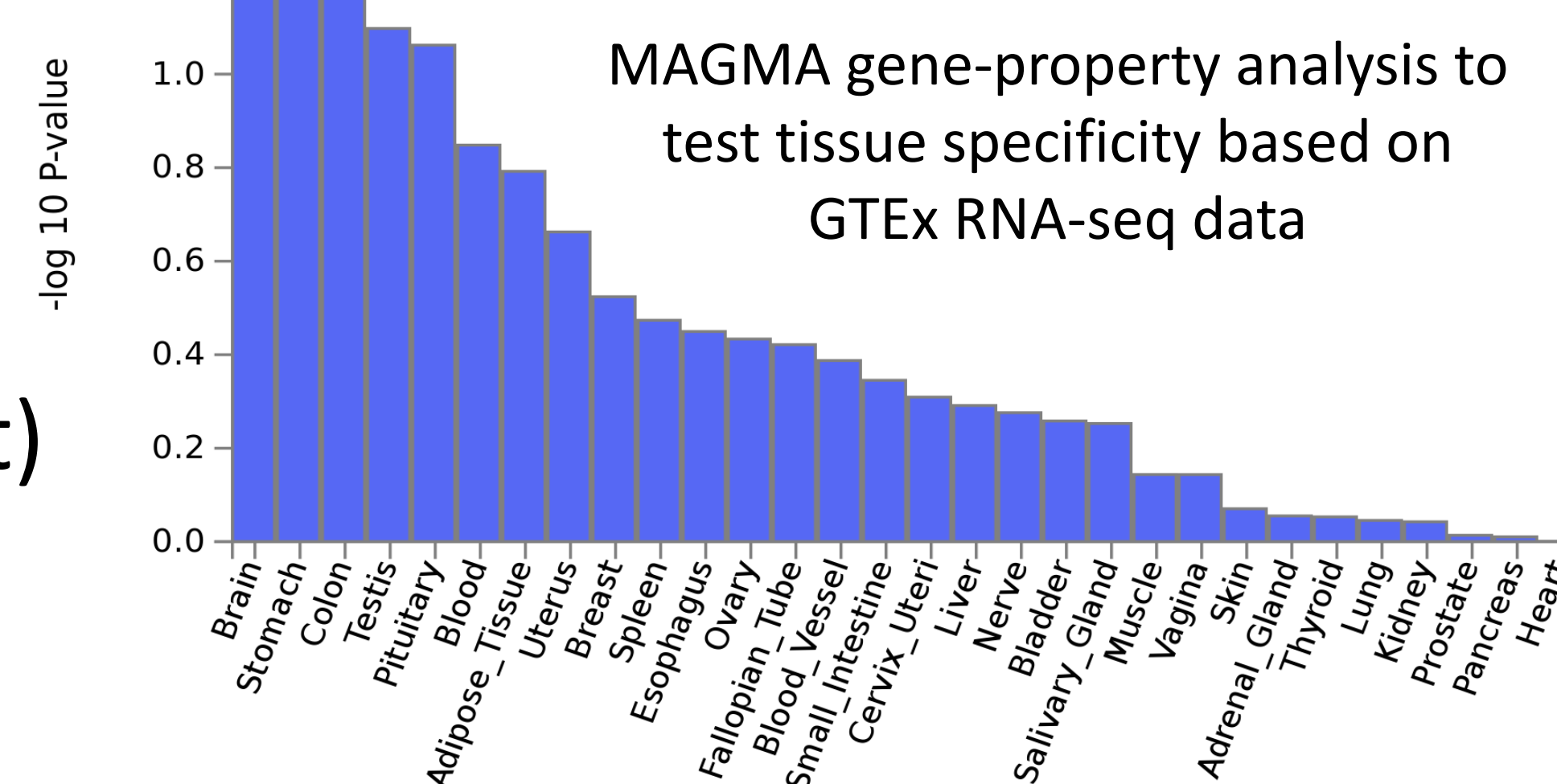
### Genetic correlations

Significant  $r_g$  with depression, schizophrenia, & wellbeing



### Enrichment

Brain areas show most enrichment (but not significant)



## NEXT STEPS

- Stratify analyses to identify homogenous genetic effects based on age, rater, or instrument
- Based on above, GenomicSEM will be used to run a common factor GWAS to examine if SNP effects act via latent genetic factor(s)
- Gene-set analyses will be performed to gain insight into specific biological pathways

## DISCUSSION

- Our study provides insight into the etiology of internalising problems
- Phenotypic heterogeneity of internalising problems is likely to underlie the lack of significant hits
- Stratified analyses will shed further light on the genetic architecture



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