



Using multimodal phenotypes in the UKB to study psychiatric conditions

Daniel Roelfs
@dthroelfs



INTRODUCTION

Psychiatric conditions are highly polygenic and complex¹

Psychiatric conditions share symptoms and genetic profiles²

MRI studies show that structural and functional changes are widespread across the brain³

Investigate distributed nature of genetic effects in the brain and its associations with psychiatric conditions

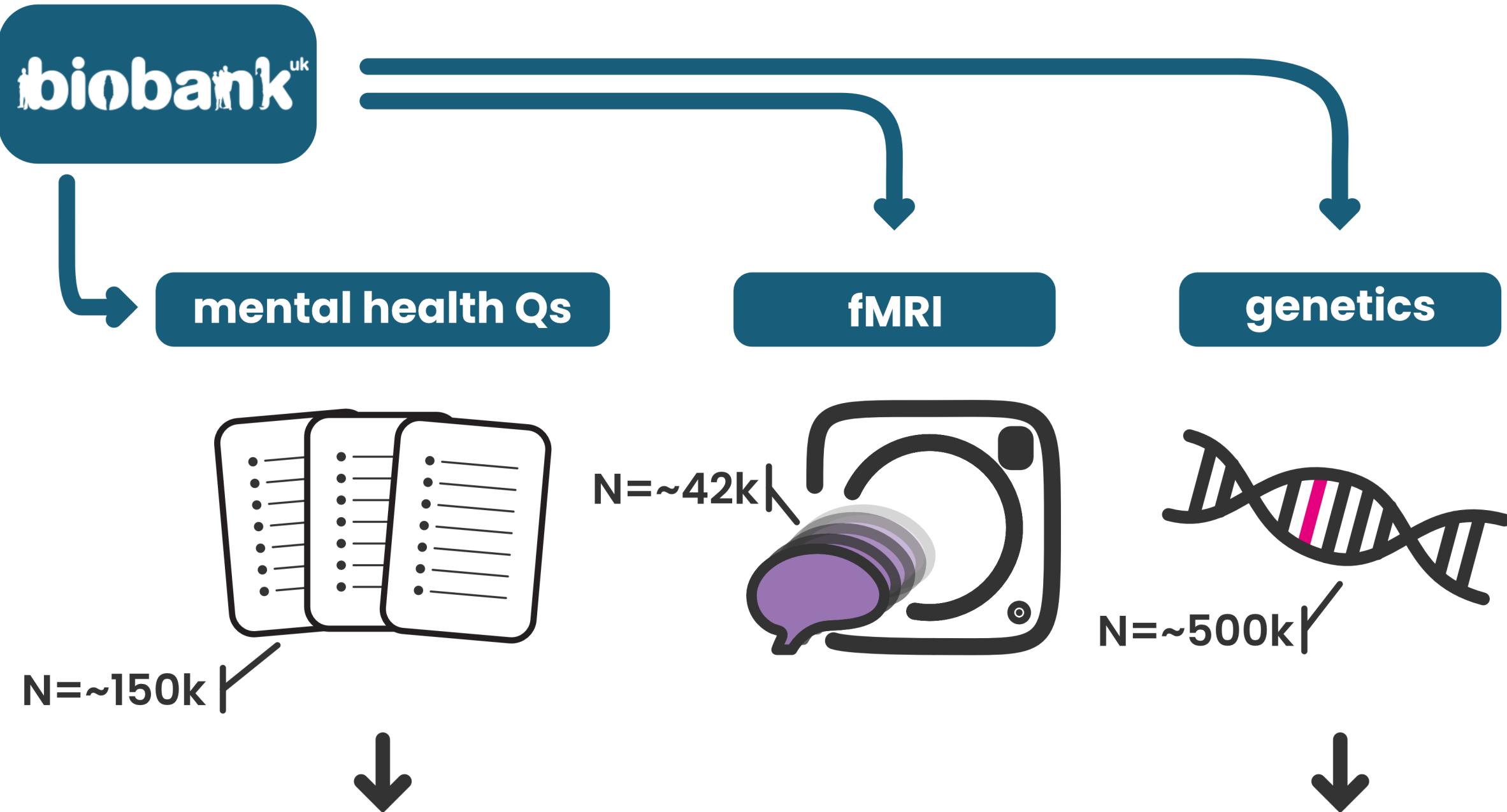
1. Anttila *et al.* *Science* (2018), Sullivan & Geschwind *Cell* (2019), Paulus & Thompson *JAMA Psychiatry* (2019)

2. Plana-Ripoll *et al.* *JAMA Psychiatry* (2019), Bulik-Sullivan *et al.* *Nature Genetics* (2015)

3. Petterson-Yeo *et al.* *Neurosci. Biobehav. Rev.* (2011), Arnatkeviciute *et al.* *NeuroImage* (2021)

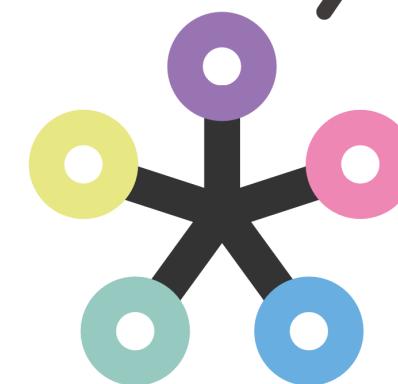
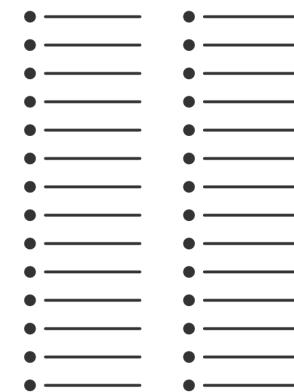
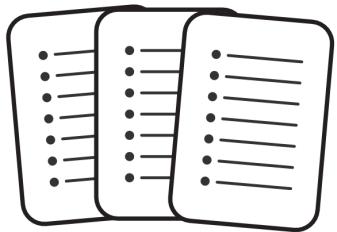


METHODS (MENTAL HEALTH)





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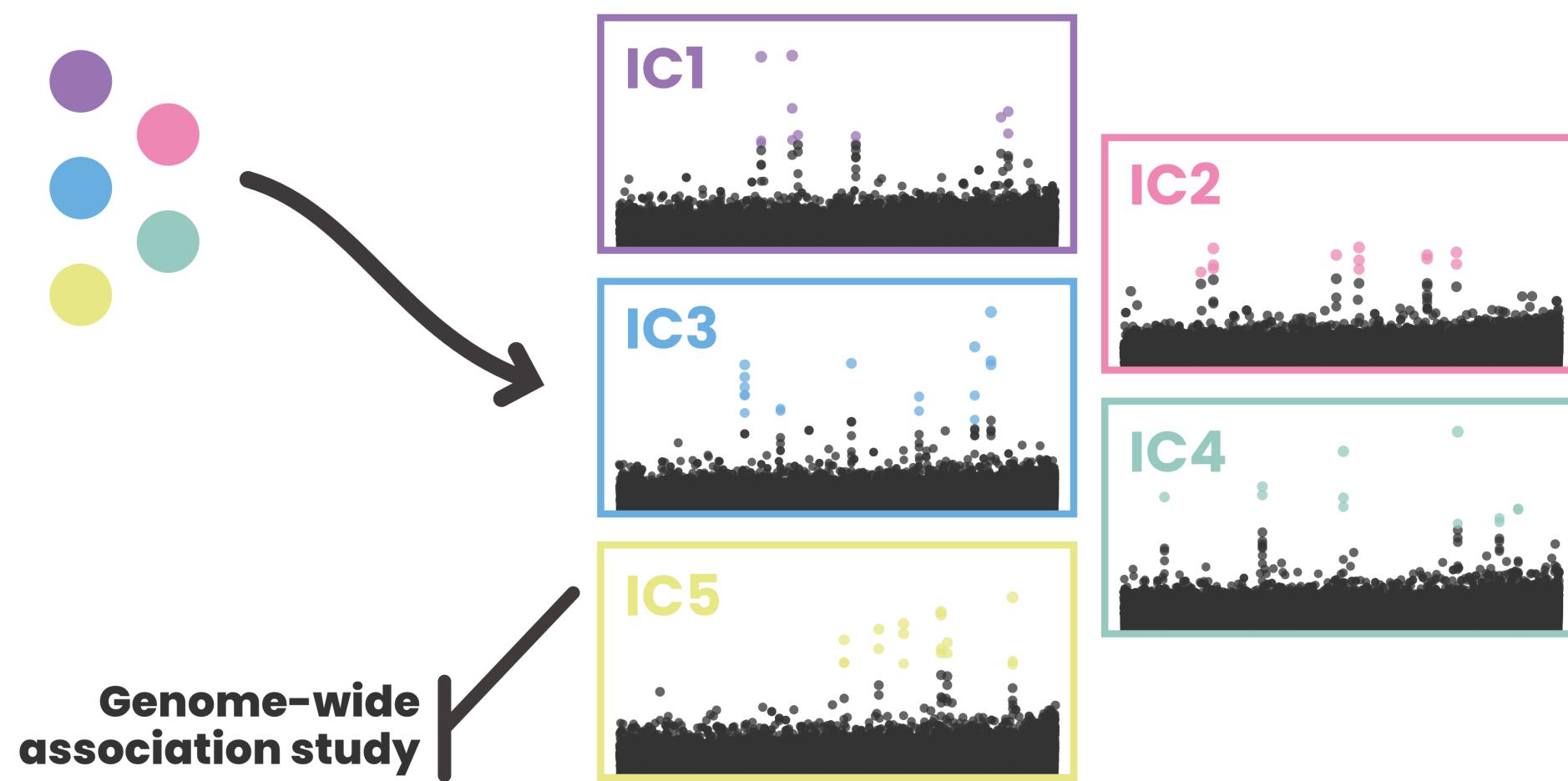
Independent Component Analysis (ICA)
dissect a set of variables
into statistically independent
components

Q1	■	■	■	■	■
Q2	■	■	■	■	■
Q3	■	■	■	■	■
Q4	■	■	■	■	■
Q5	■	■	■	■	■
Q6	■	■	■	■	■
Q7	■	■	■	■	■
Q8	■	■	■	■	■
Q9	■	■	■	■	■
Q _n	■	■	■	■	■
	IC1	IC2	IC3	IC4	IC5



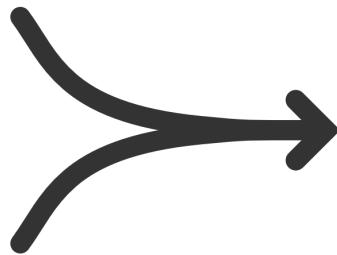
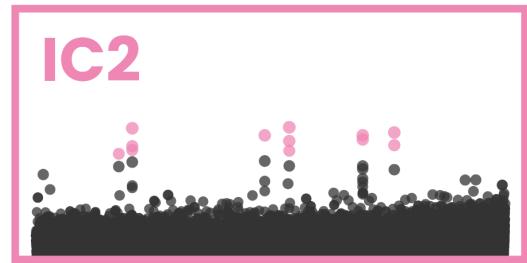
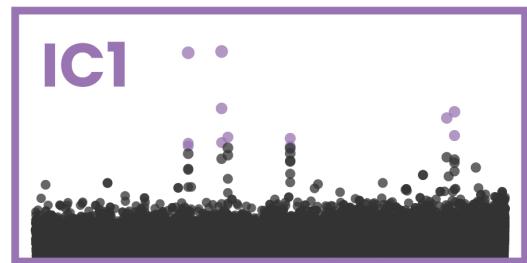


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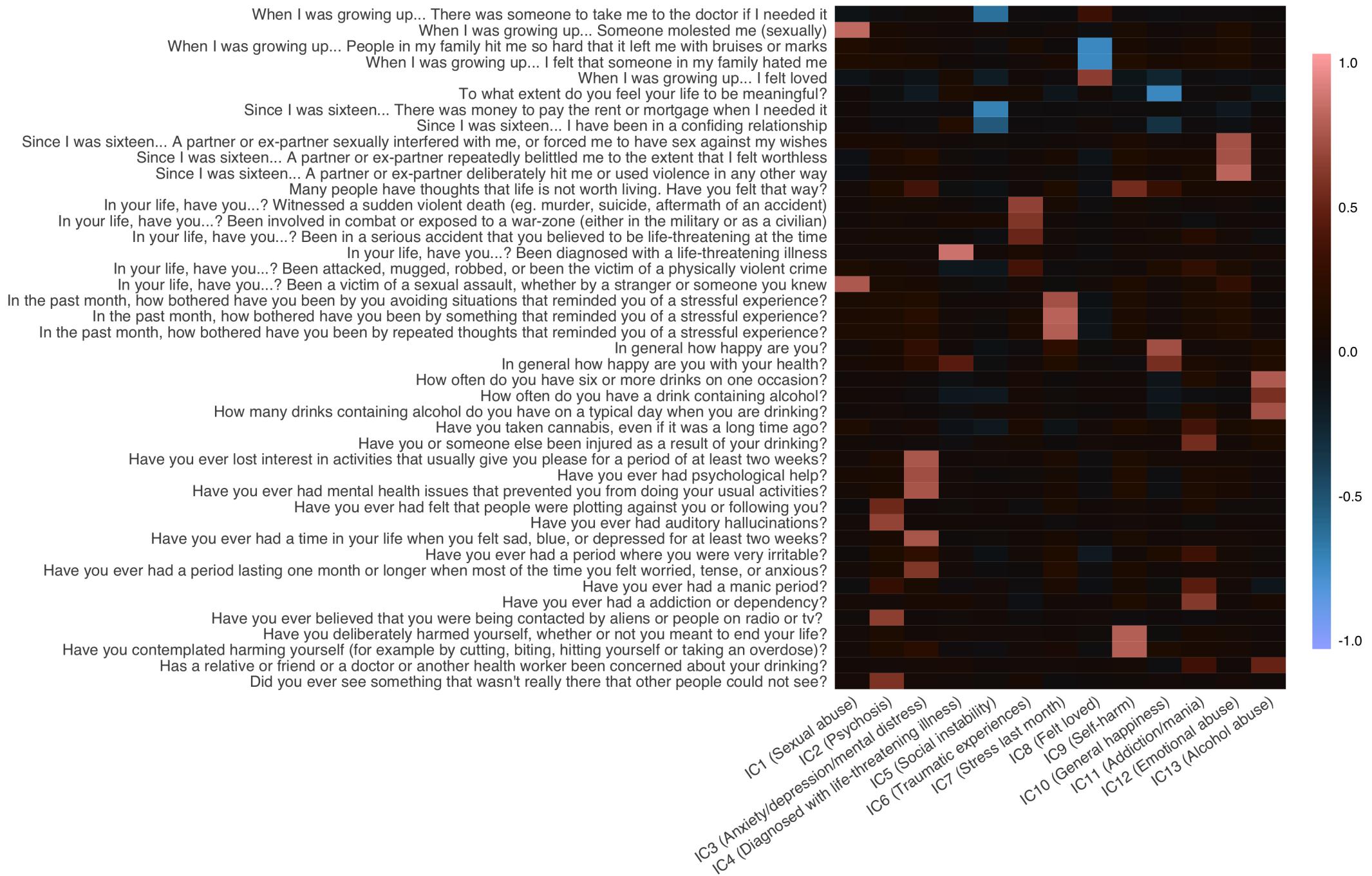


	IC1	IC2	IC3	IC4	IC5
IC5					X
IC4				X	
IC3			X		
IC2		X			
IC1	X				

LD Score Regression
quantifies genetic correlation
between two traits

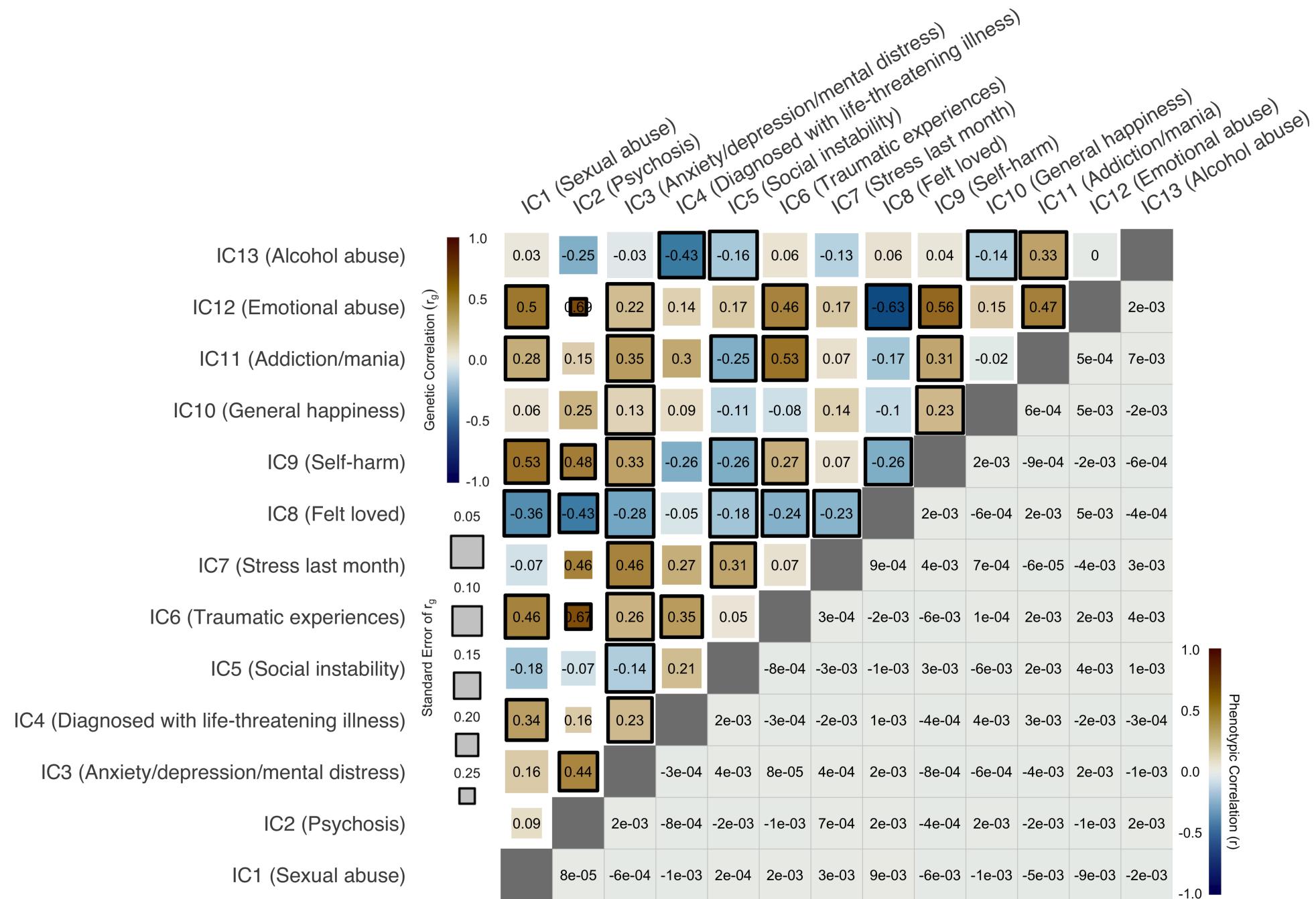


RESULTS (ICA DECOMPOSITION)



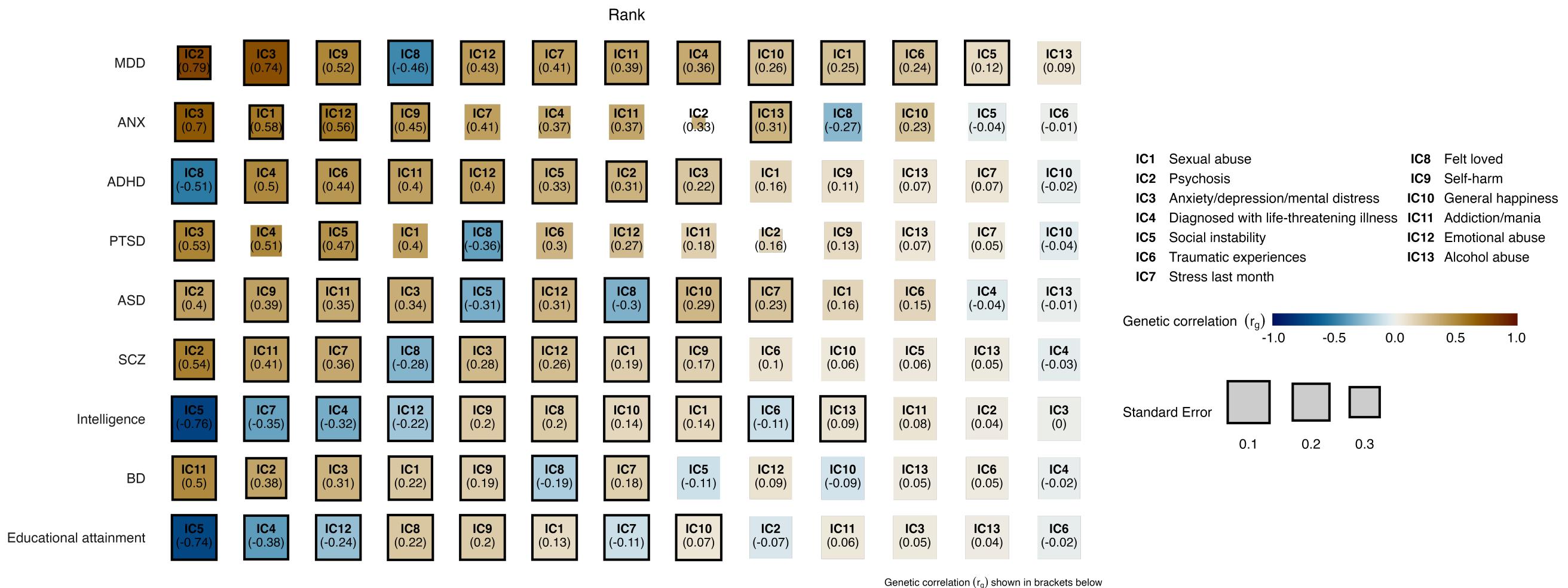


RESULTS (IC X IC)



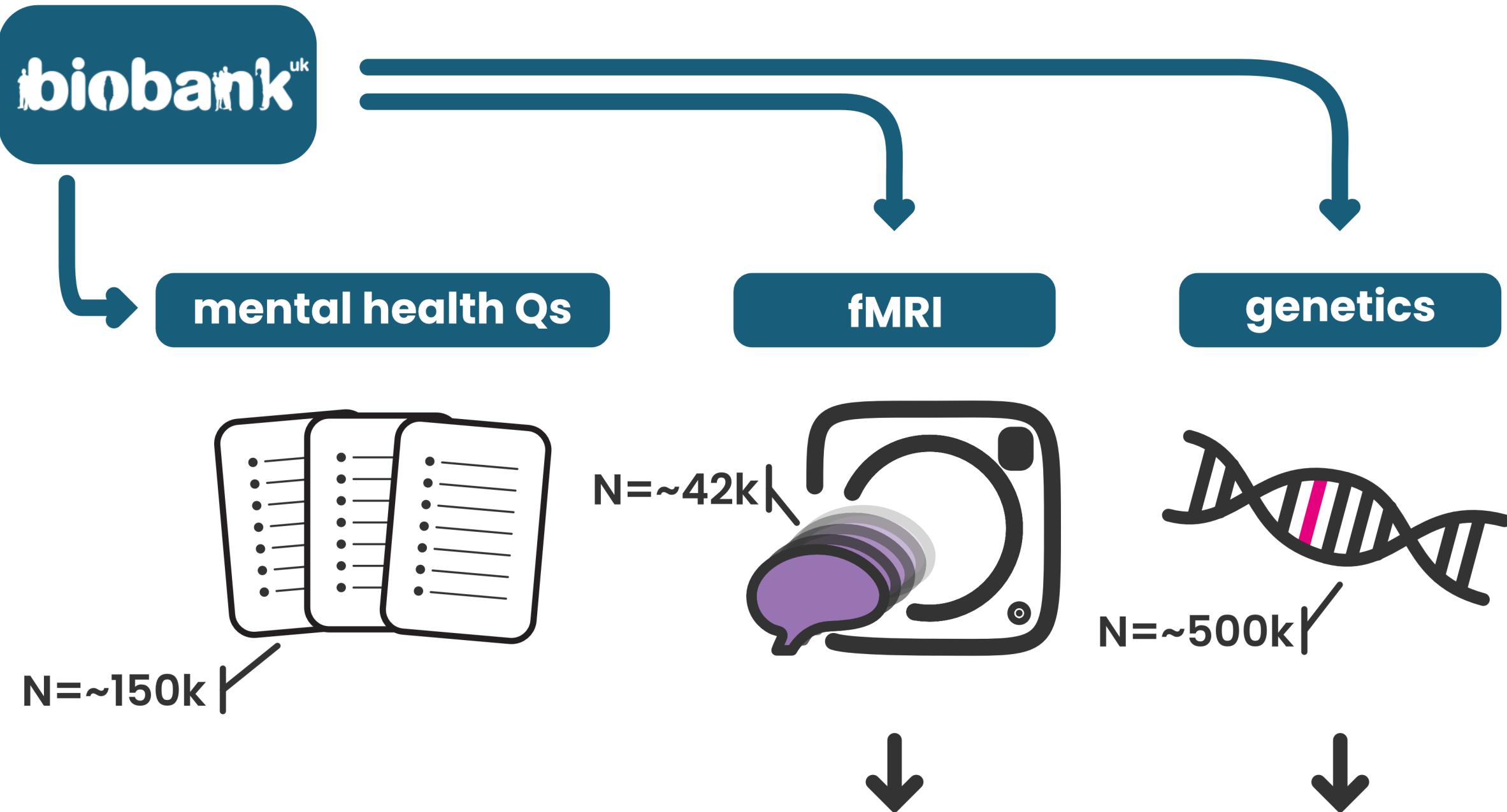


RESULTS (IC X IC)



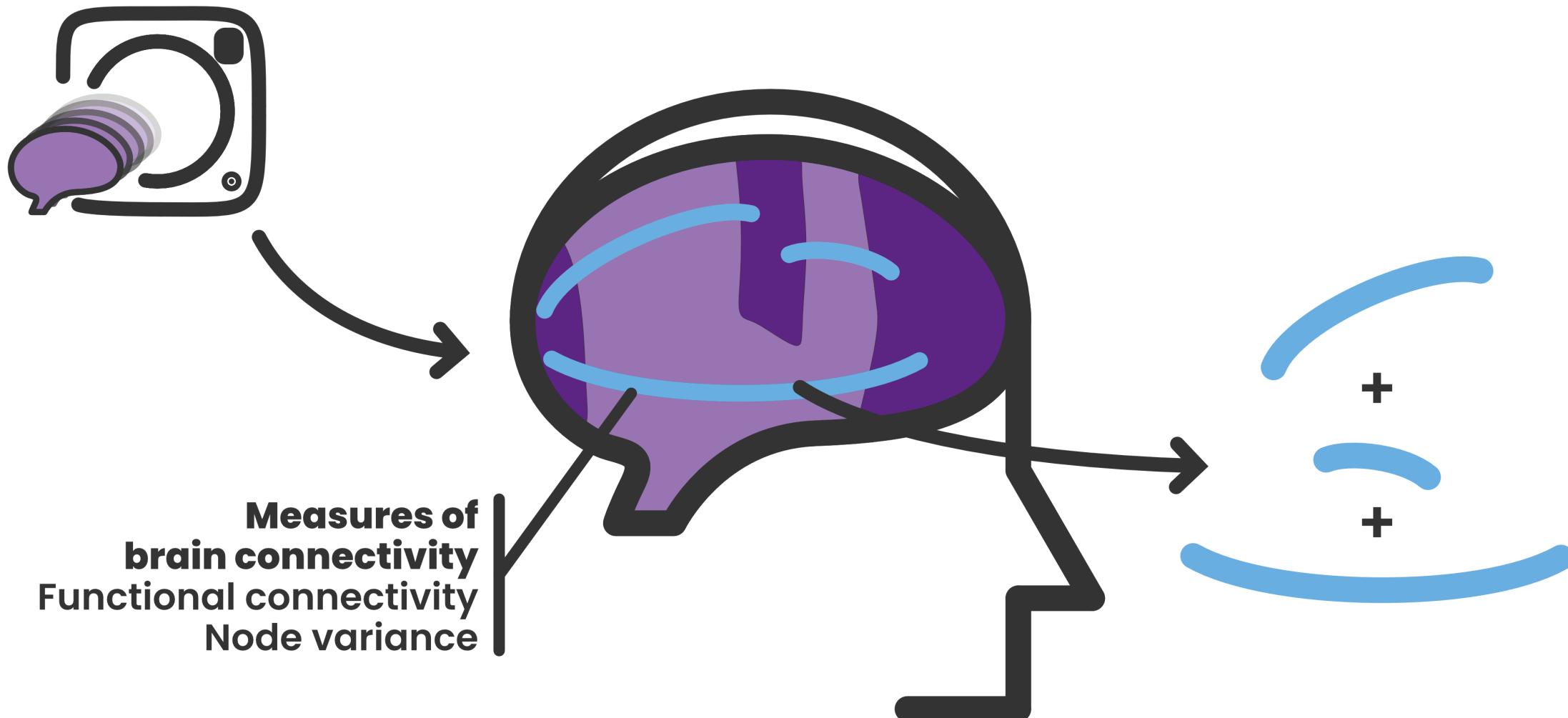


METHODS (fMRI)





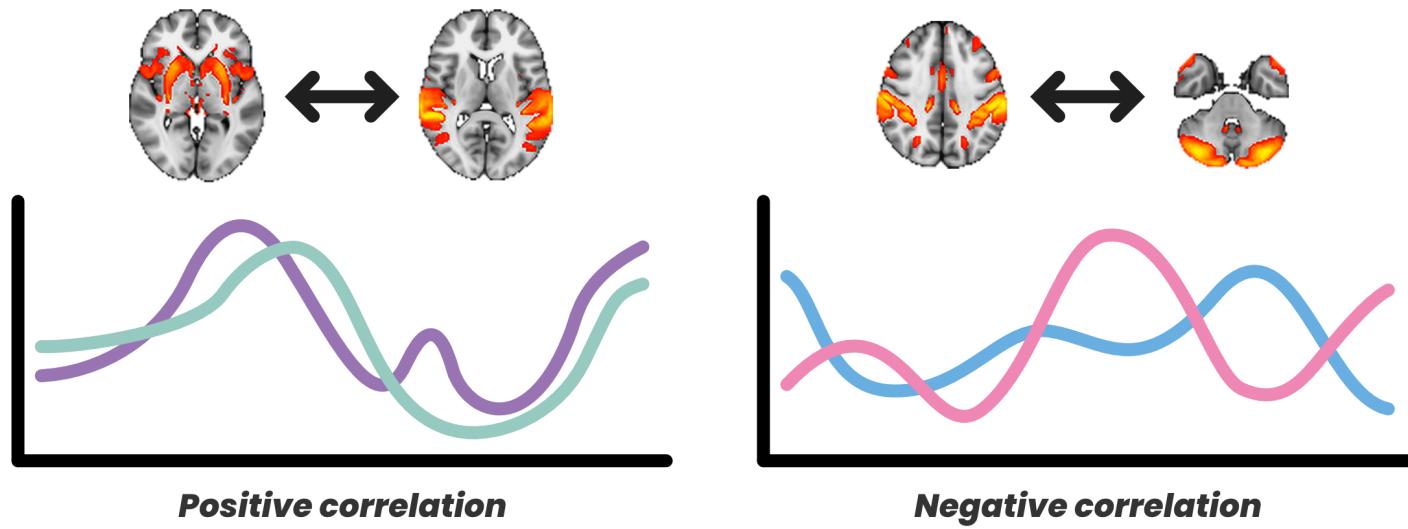
METHODS (fMRI)



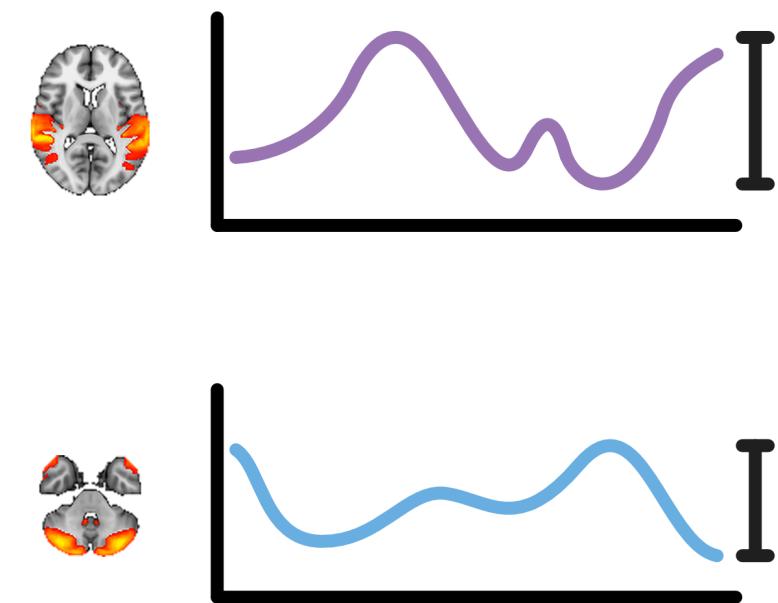


BRAIN CONNECTIVITY MEASURES

Functional Connectivity

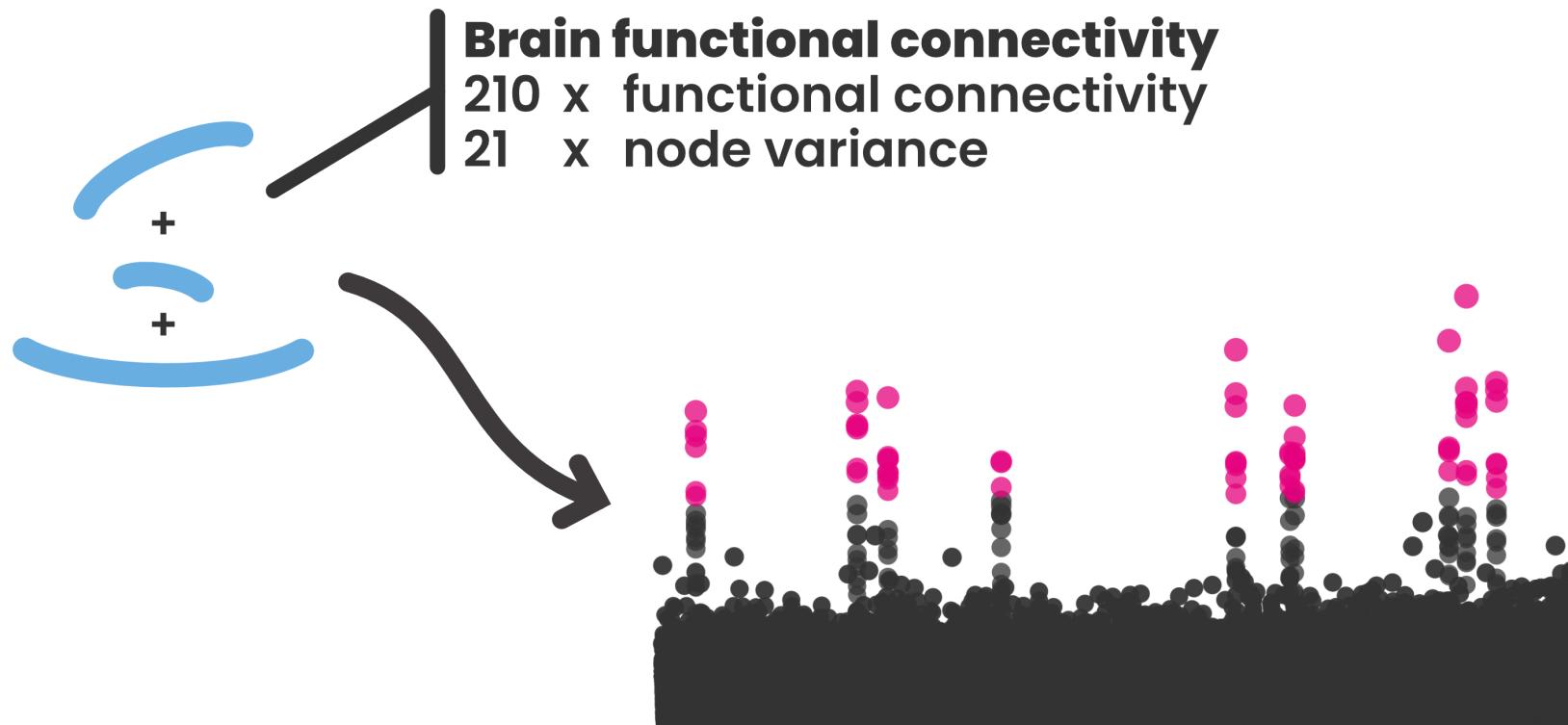


Temporal node variance



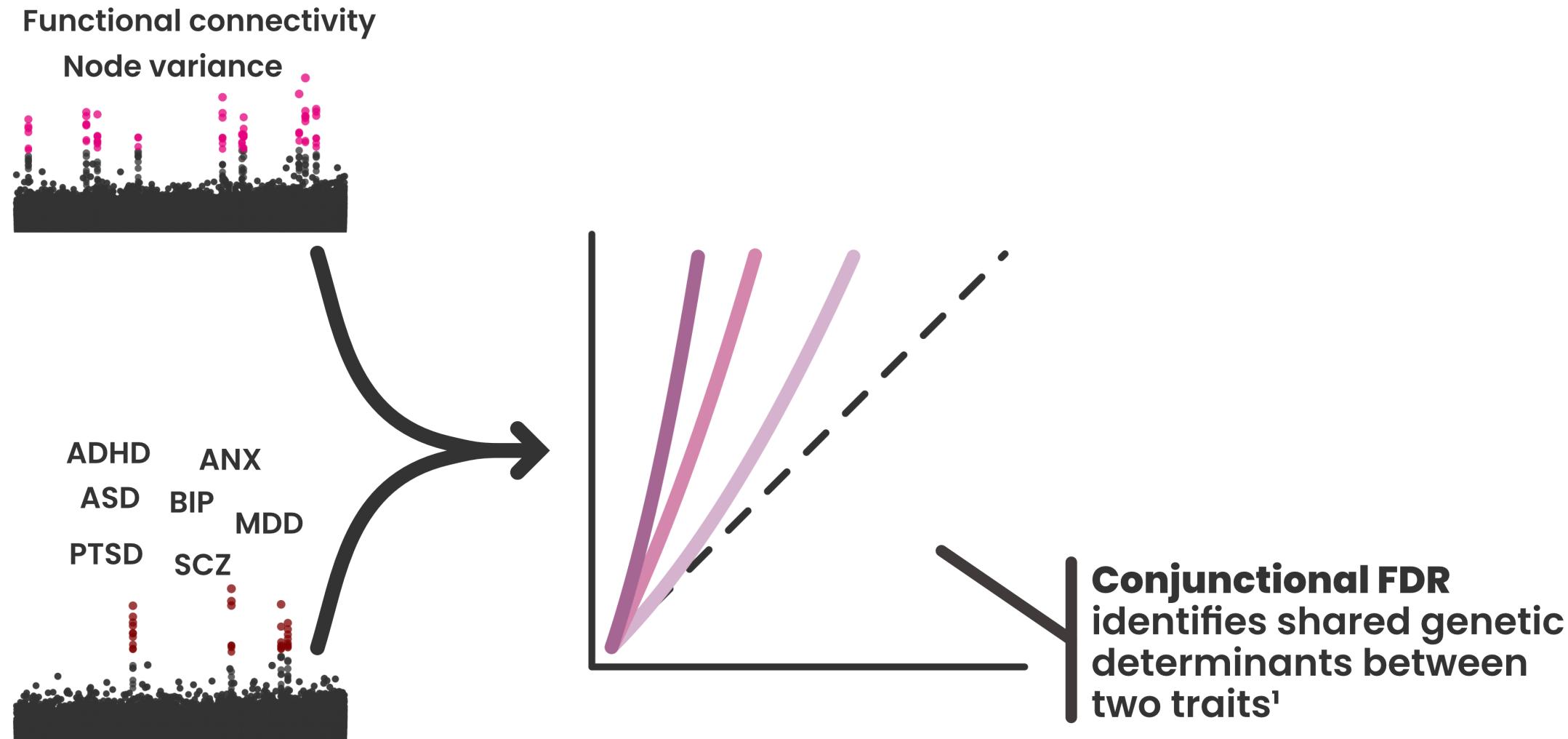


METHODS (fMRI)





METHODS (fMRI)



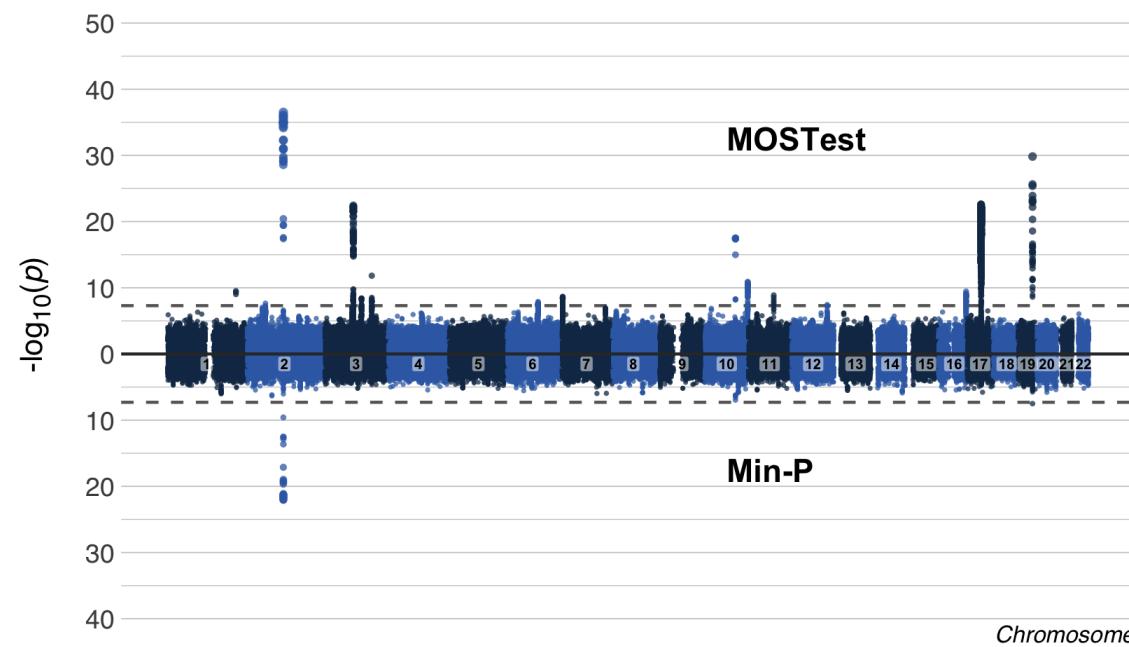


MOSTEST MANHATTAN PLOTS

Functional Connectivity

MOSTest 15 loci

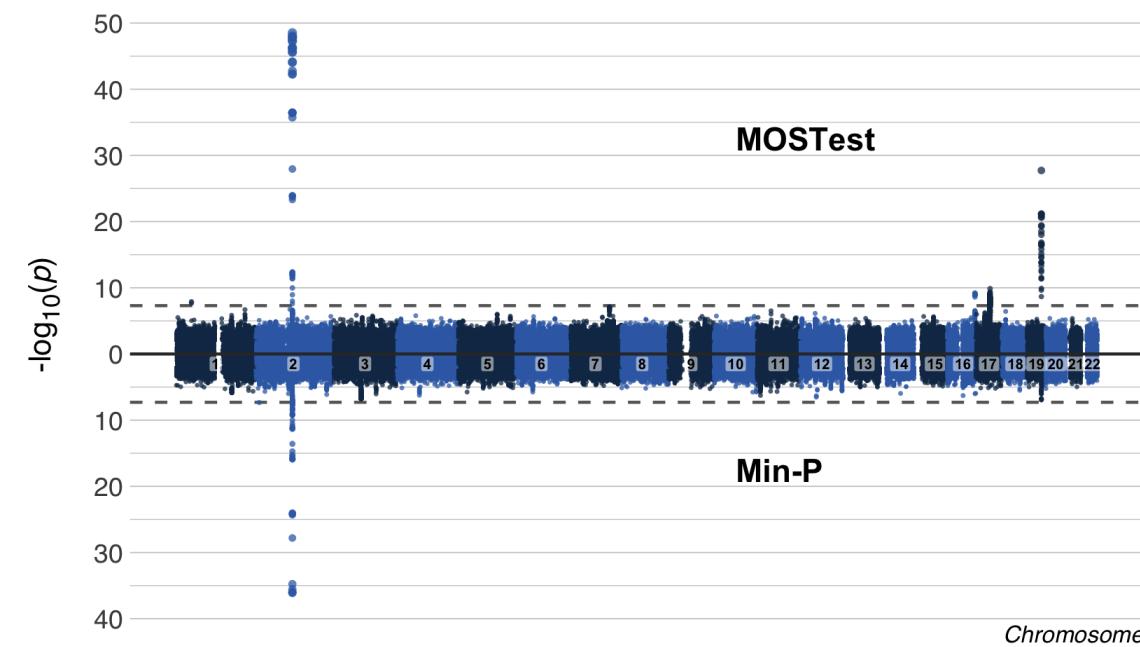
Min-P 2 loci



Temporal Node Variance

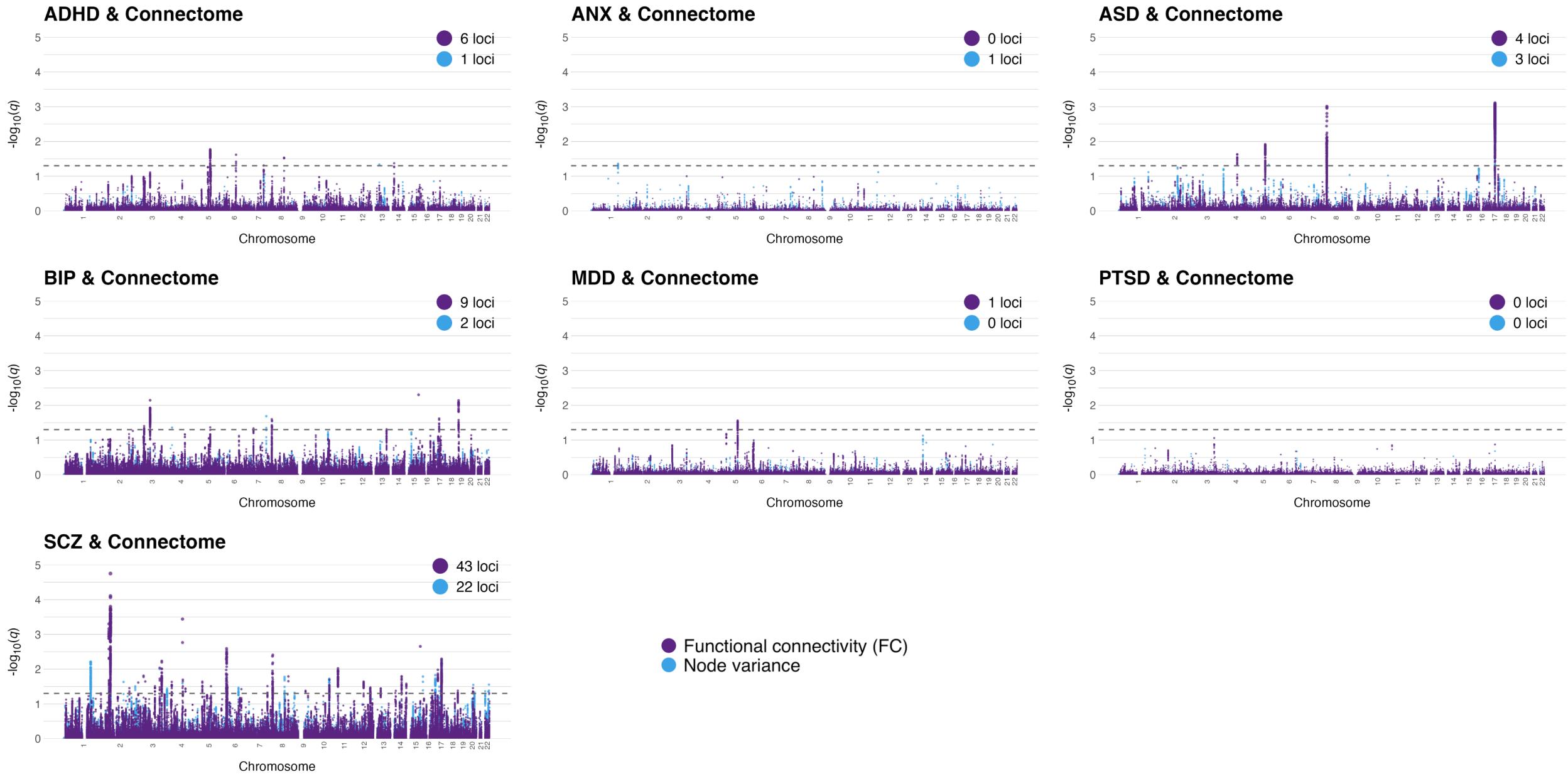
MOSTest 5 loci

Min-P 3 loci





CONJUNCTIONAL FDR





MAPPED GENES

Functional annotation and mapping of genome-wide association studies (FUMA)¹



Gene set mapped from the significant loci in the GWAS



Compare identified genes to genes involved in synapses (e.g. BDNF, NRXN1 etc.)²

1. Watanabe *et al.* *Nature Communications* (2017)

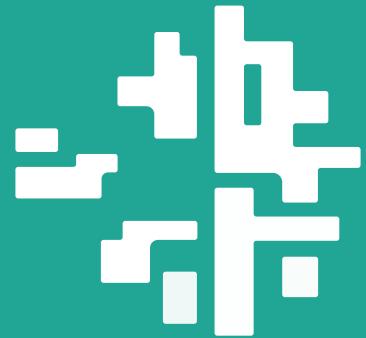
2. SynGO, Koopmans *et al.* *Neuron* (2019)



CONCLUSION

- ☒ Pleiotropy between mental health symptom profiles, functional connectivity, and psychiatric conditions
- ▣ Link genetic loci back to biological processes implicated in psychiatric conditions
- ⌚ Identified a number of synaptic processes associated with these shared loci

Thank you!



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