



# Shared Genetic Determinants Between the Brain Functional Connectome and Psychiatric Disorders

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***No disclosures to declare***



## BACKGROUND

Psychiatric conditions are highly polygenic and complex<sup>1</sup>

Psychiatric conditions share symptoms and genetic profiles<sup>2</sup>

MRI studies show that structural and functional changes are widespread across the brain<sup>3</sup>

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

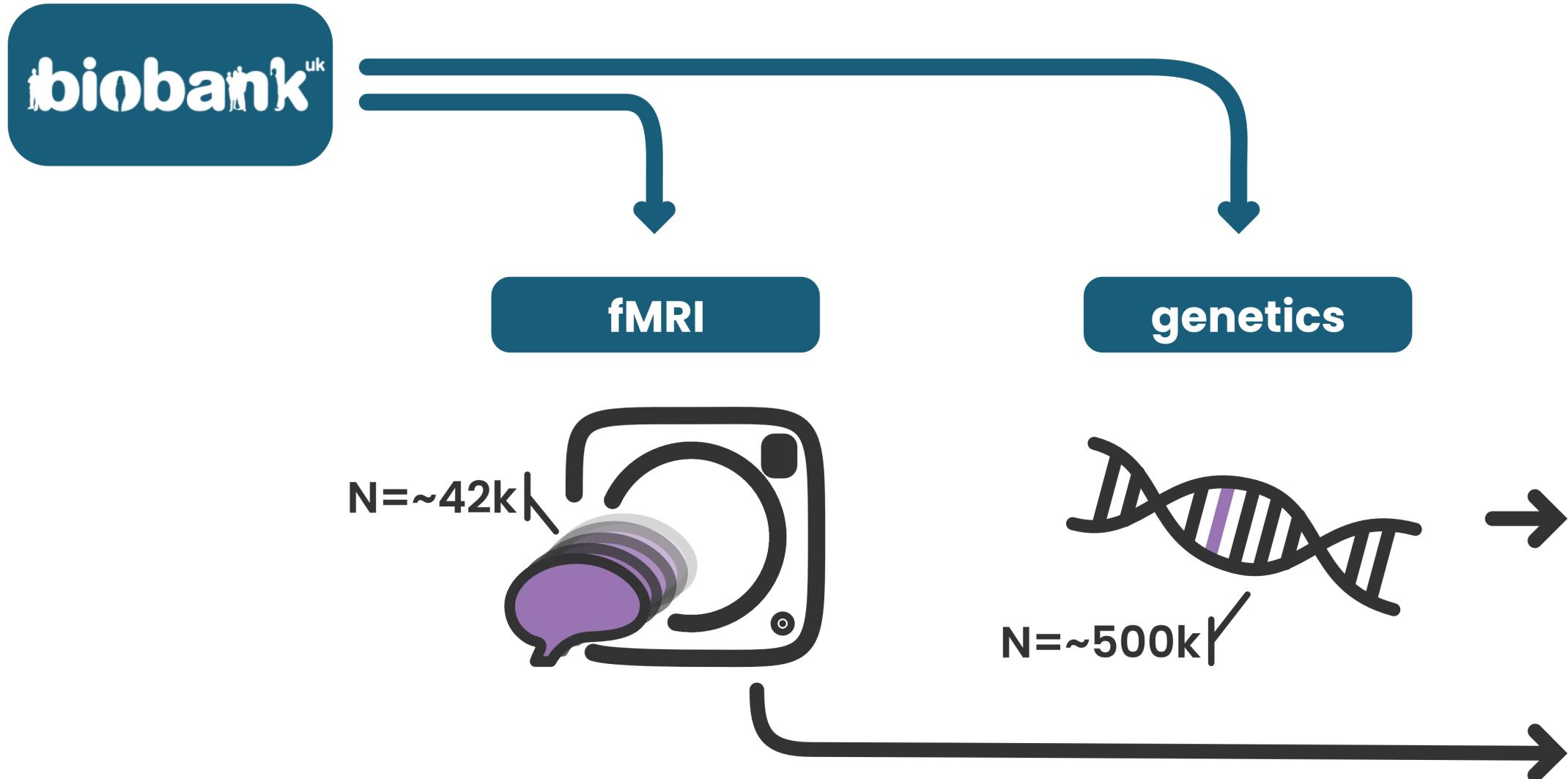
1. Anttila *et al.* Science (2018), Sullivan & Geschwind Cell (2019), Paulus & Thompson JAMA Psychiatry (2019)

2. Plana-Ripoll *et al.* JAMA Psychiatry (2019), Roelfs *et al.* Transl. Psychiatry (2021)

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



## DATASET





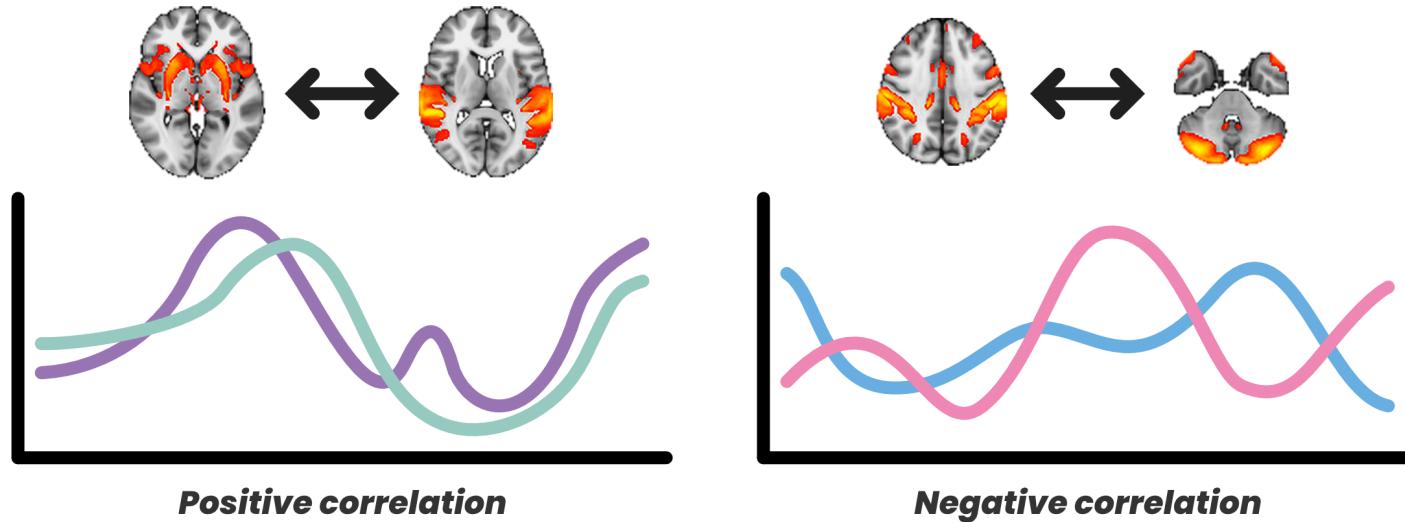
## BRAIN CONNECTIVITY MEASURES



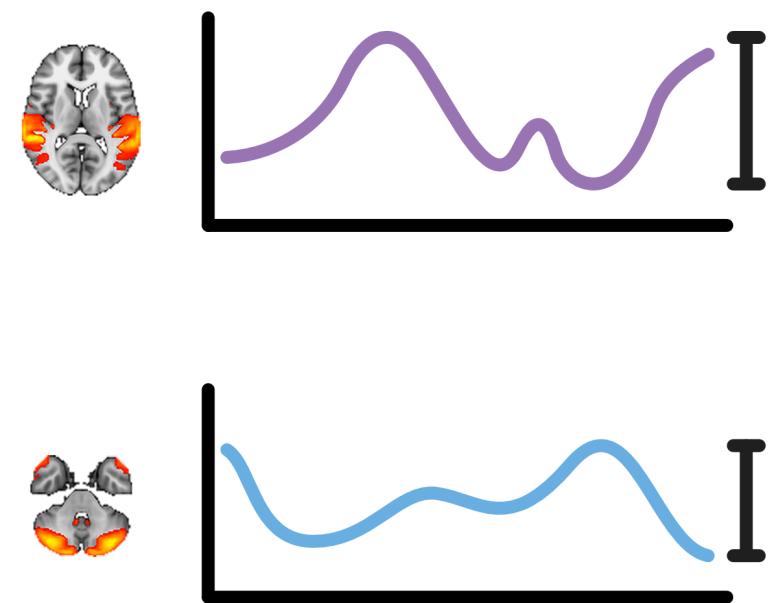


## BRAIN CONNECTIVITY MEASURES

### Functional Connectivity

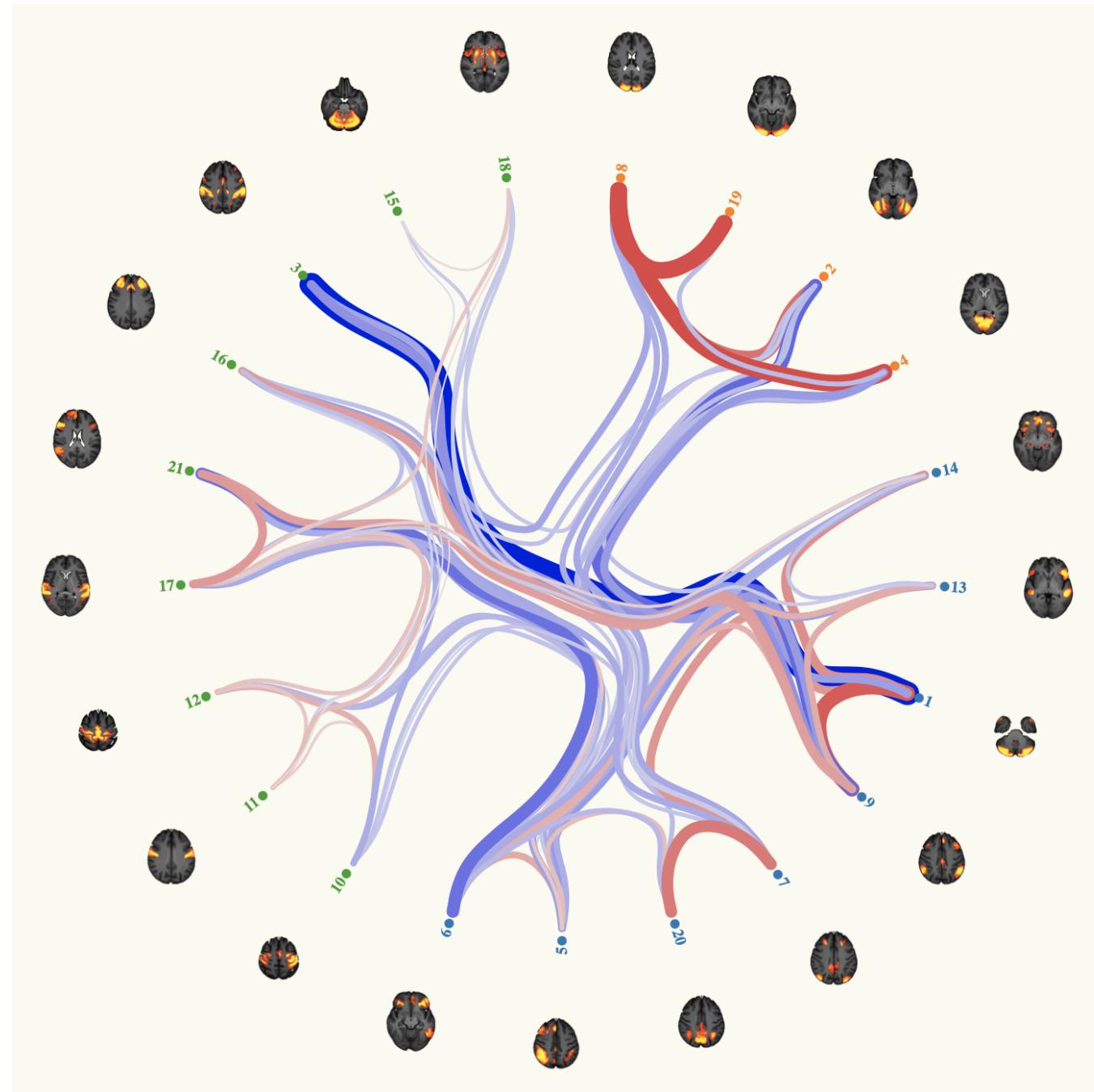


### Temporal node variance





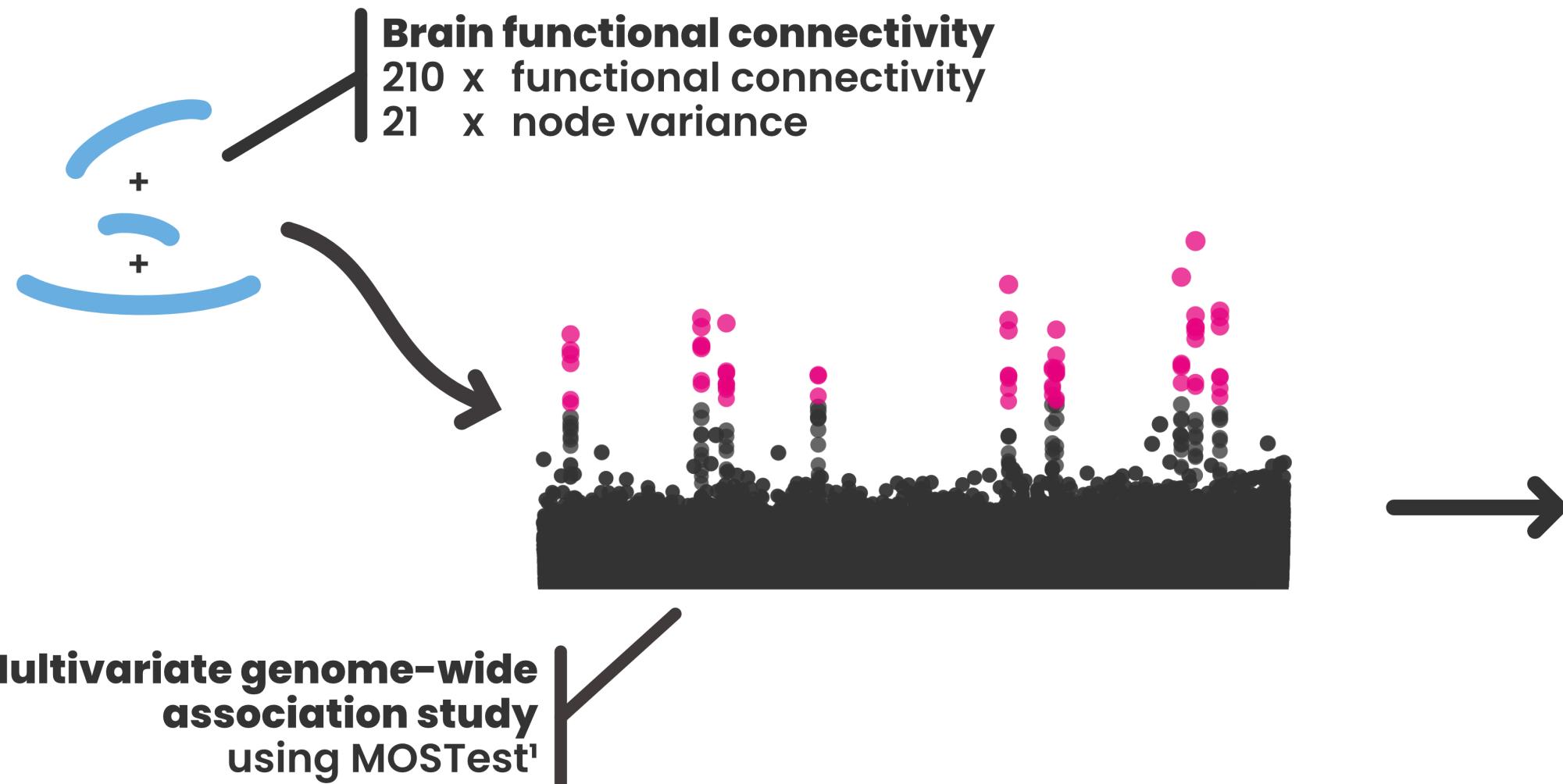
# BRAIN FUNCTIONAL CONNECTIVITY



UK Biobank Brain Imaging - Connectome Browser (d25)



## MULTIVARIATE GWAS



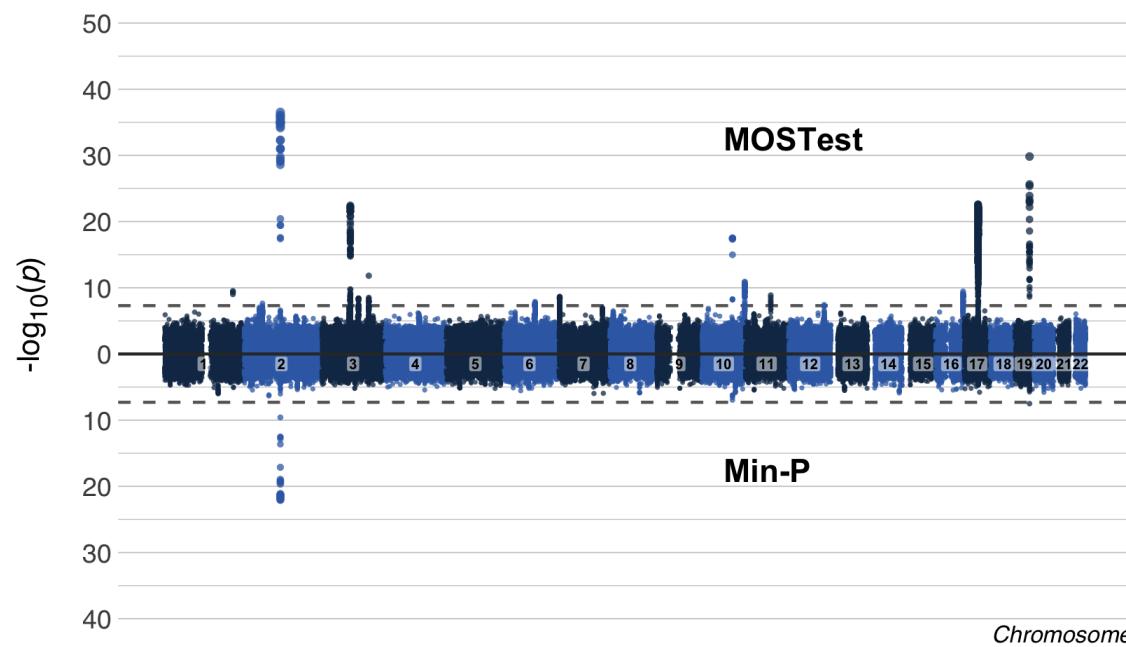


## MOSTEST MANHATTAN PLOTS

### Functional connectivity

**MOSTest** 15 loci

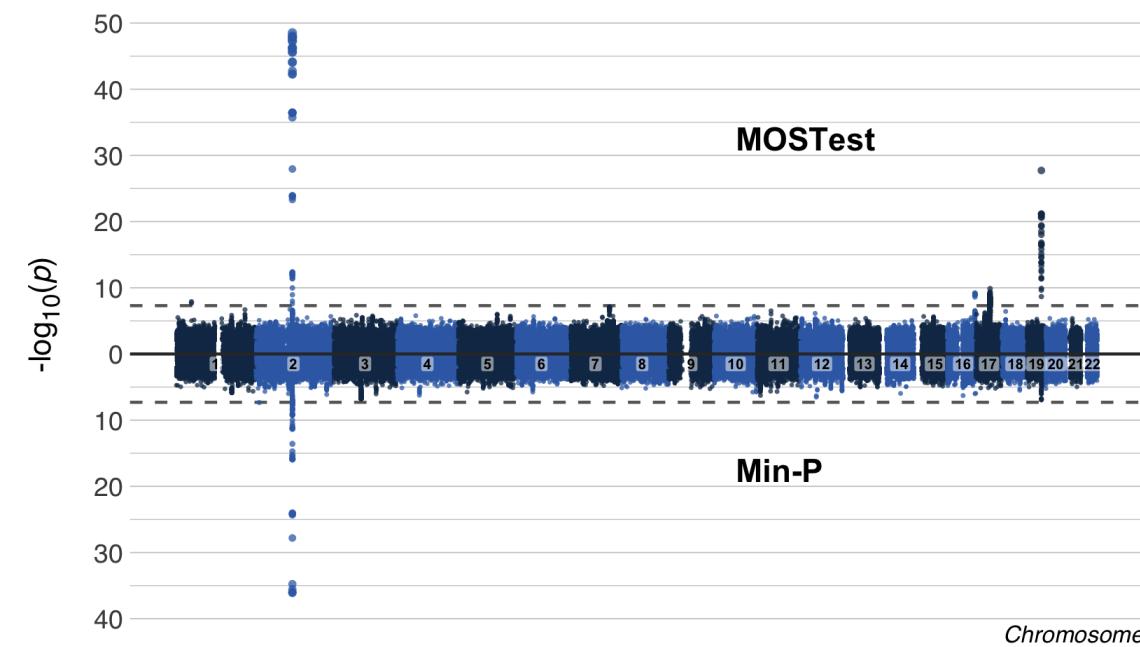
**Min-P** 2 loci



### Node variance

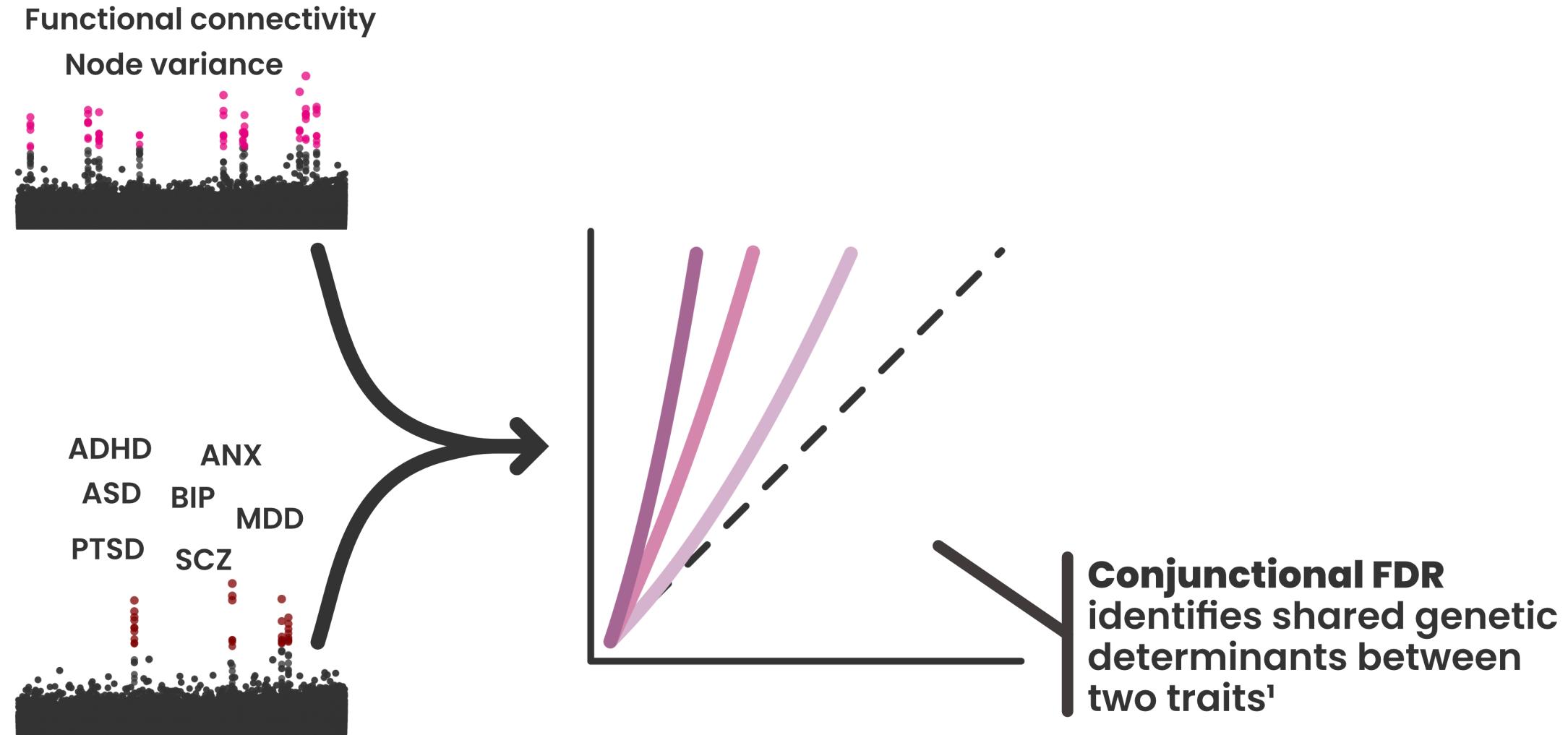
**MOSTest** 5 loci

**Min-P** 3 loci



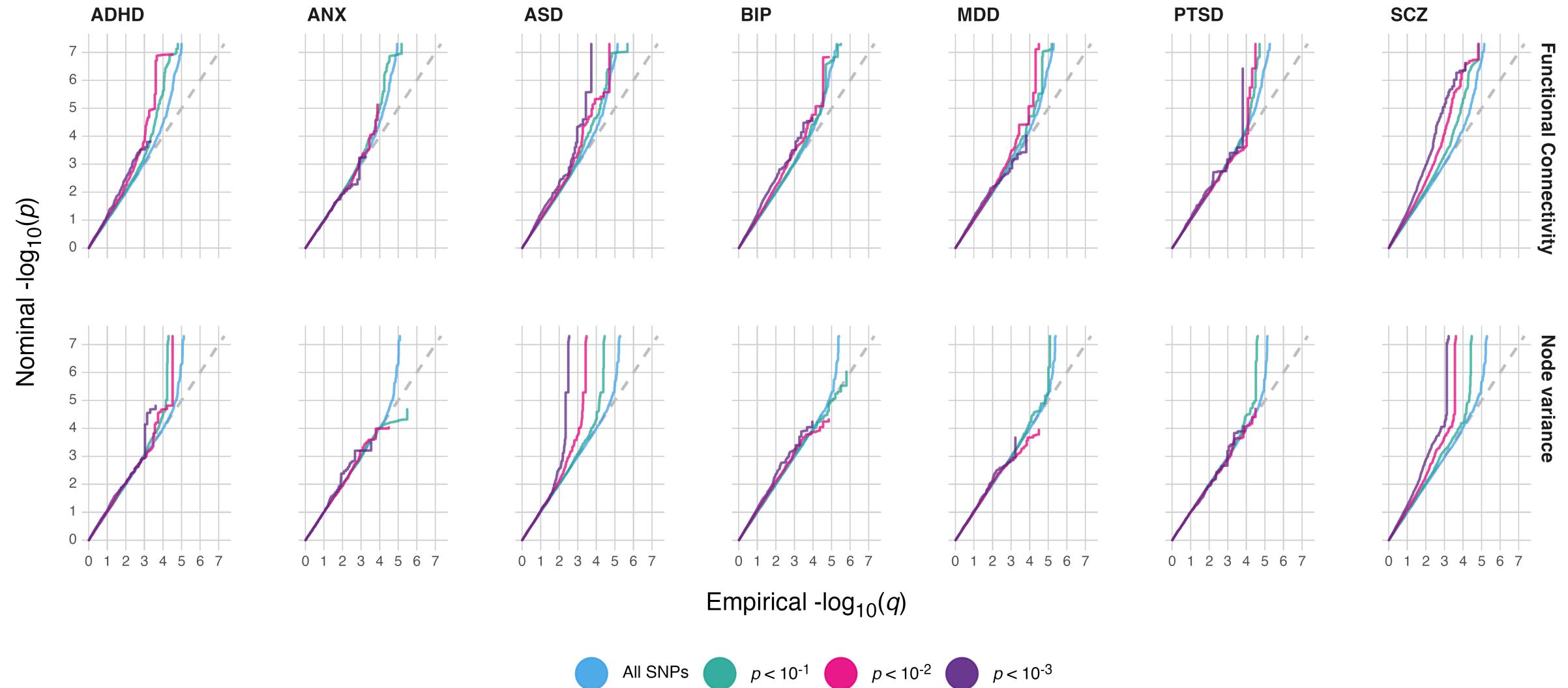


## GENETIC OVERLAP



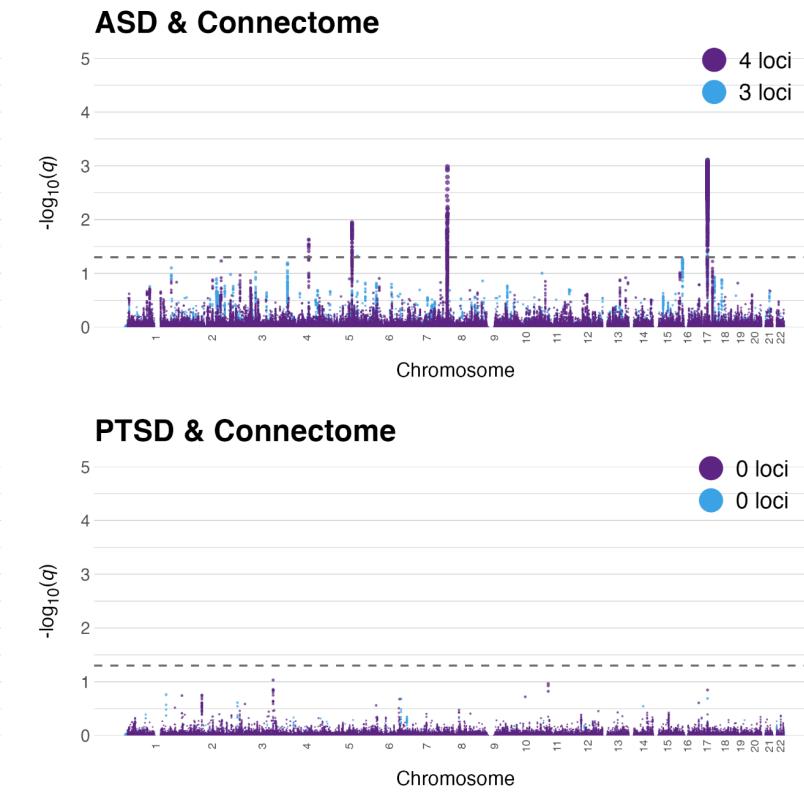
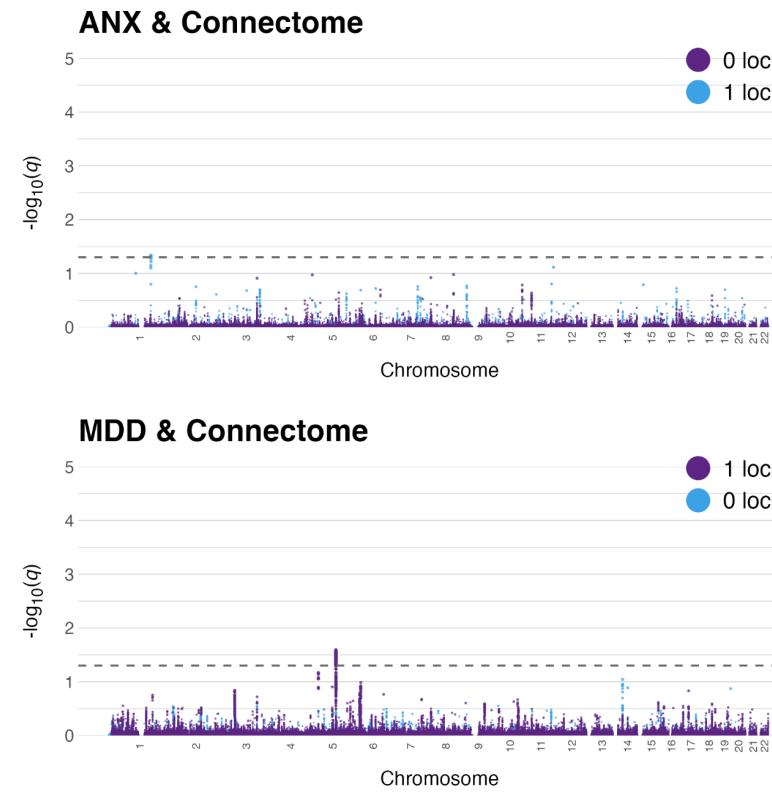
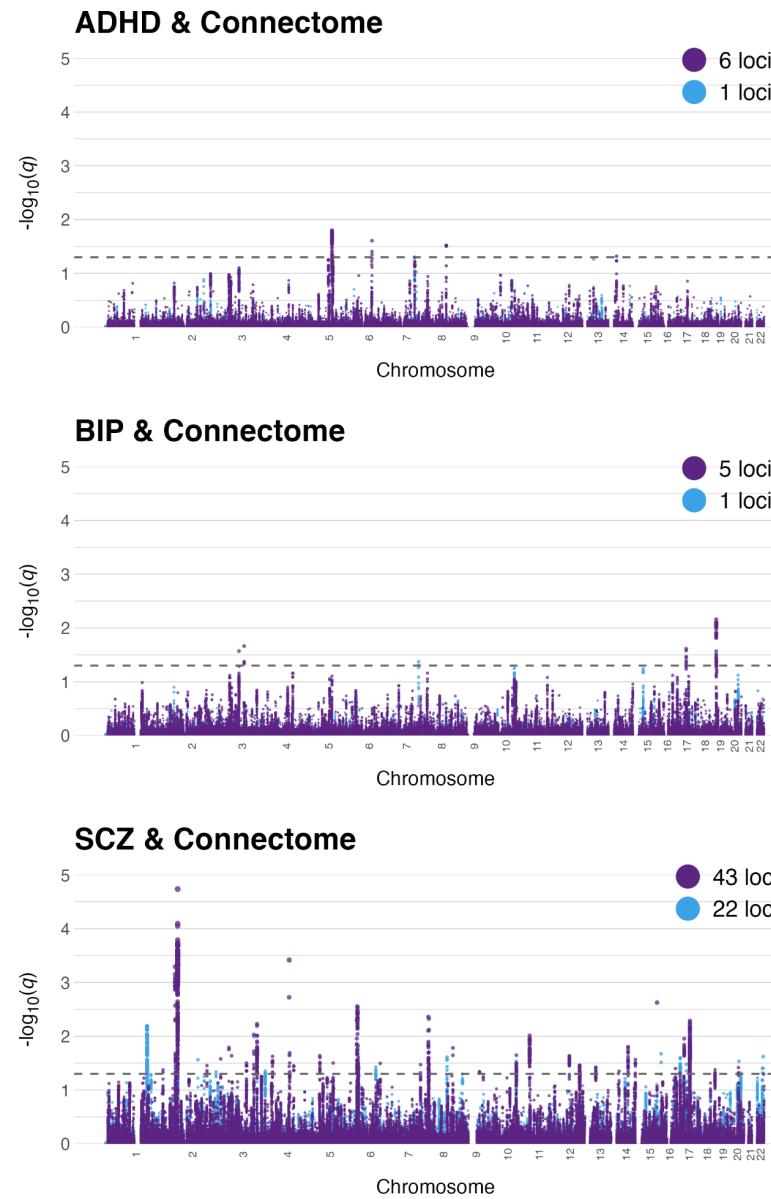


## CONJUNCTIONAL FDR





# CONJUNCTIONAL FDR



● Functional connectivity (FC)  
● Node variance



## MAPPED GENES

Functional annotation and mapping of genome-wide association studies (FUMA<sup>1</sup>)



Gene set mapped from the significant loci in the GWAS



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

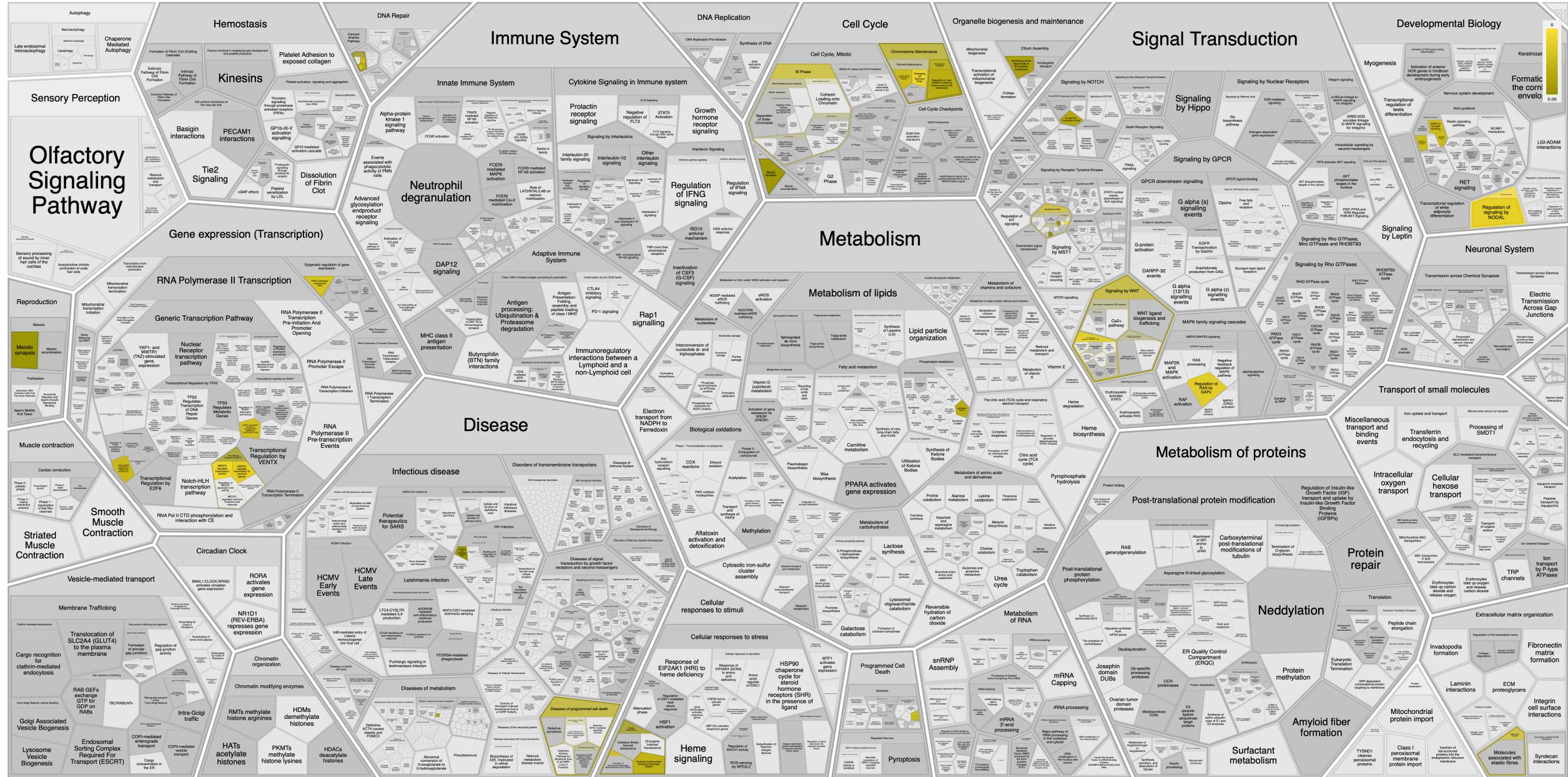


1. Watanabe *et al.* *Nature Communications* (2017)

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



# MAPPED BIOLOGICAL PROCESSES





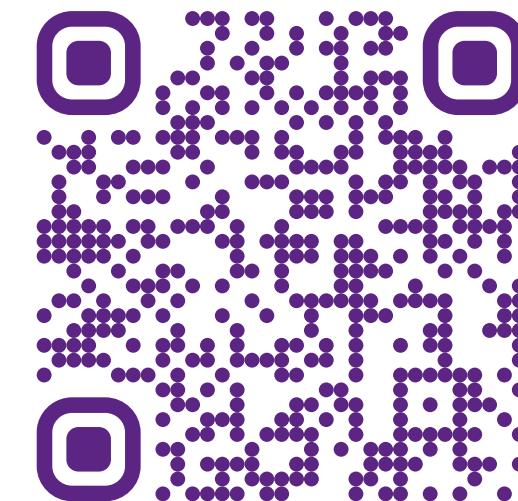
## CONCLUSION

- ☒ Genetic overlap between functional connectivity and psychiatric conditions
- 🧠 Link genetic loci back to biological processes implicated in psychiatric conditions
- /gpl Identified a number of synaptic processes associated with shared loci

### Genetic overlap between multivariate measures of human functional brain connectivity and psychiatric disorders

Daniel Roelfs, Dennis van der Meer, Dag Alnæs, Oleksandr Frei, Robert Loughnan, Chun Chieh Fan, Anders M. Dale, Ole A. Andreassen, Lars T. Westlye, Tobias Kaufmann  
doi: <https://doi.org/10.1101/2021.06.15.21258954>

This article is a preprint and has not been certified by peer review [what does this mean?]. It reports new medical research that has yet to be evaluated and so should not be used to guide clinical practice.



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Abstract

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Abstract

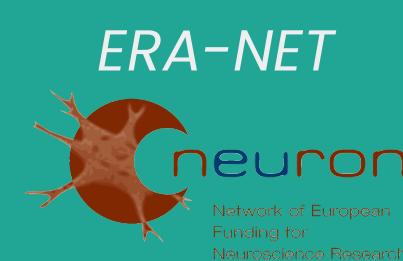


UiO : University of Oslo



Thanks to

biobank<sup>uk</sup>



**SYNSCHIZ**

Linking synaptic dysfunction to  
disease mechanisms in  
schizophrenia

