

Widespread associations between grey-matter structure and the human phenotype

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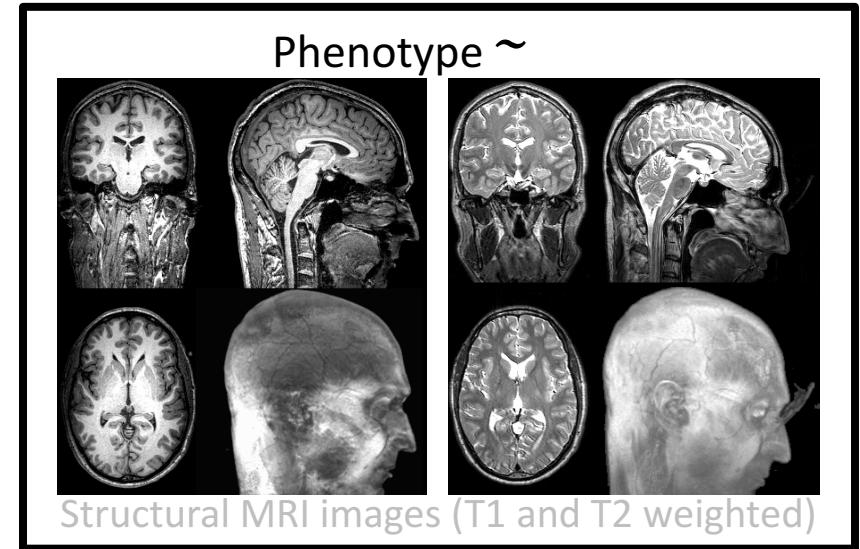
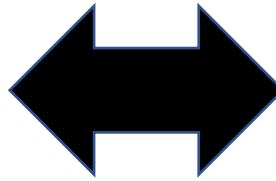
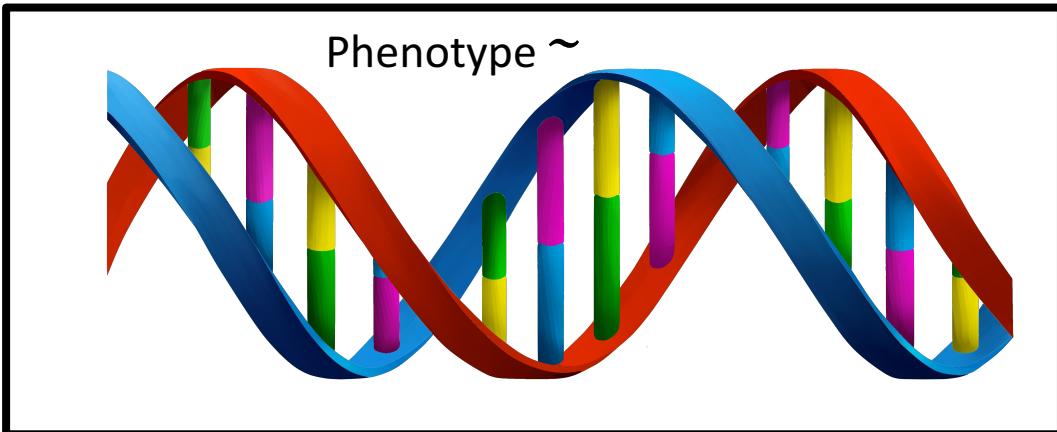
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Program in Complex
Trait Genomics



From genetics to MRI analyses

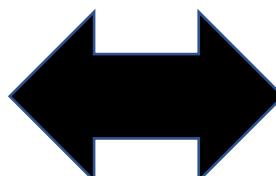


How to make inference from the large samples but even larger number of measurements?

SNP heritability

rG: genetic correlation

Polygenic Risk Score

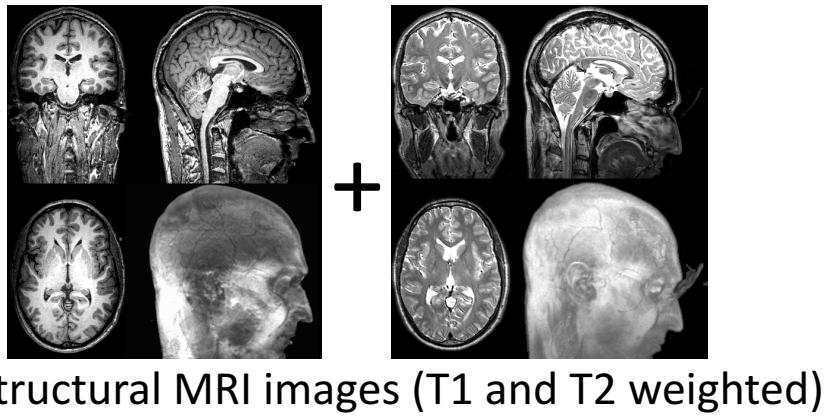


Brain morphometricity (Sabuncu et al., 2016)
association with all brain vertices

rGM: grey-matter correlation

Grey-matter score

Grey-matter structure measurements



FreeSurfer 6.0



Surface-based representation

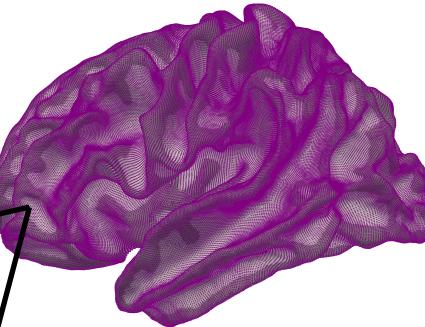
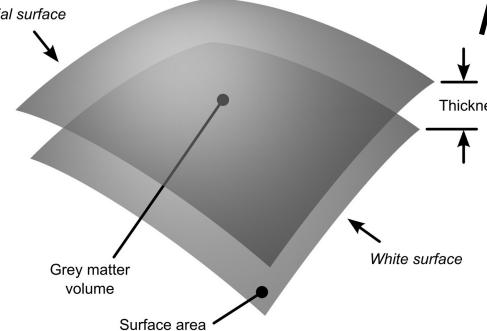
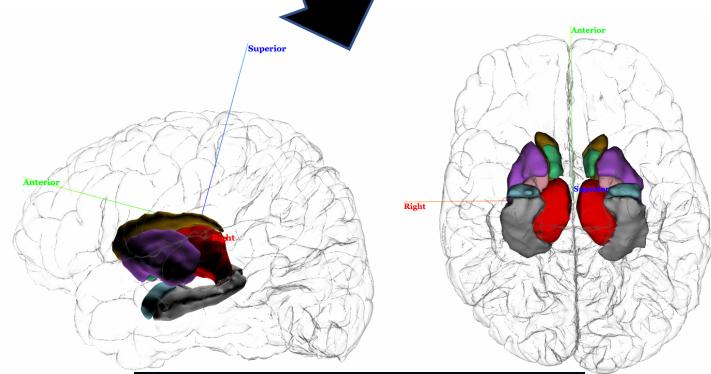


Figure adapted from
Winkler et al., 2010

Vertex-wise
measurements of
cortical surface &
thickness



Gutman et al., 2013 & 2015

<http://enigma.ini.usc.edu/protocols/imaging-protocols/>

Vertex-wise
measurements of
subcortical
thickness and
area

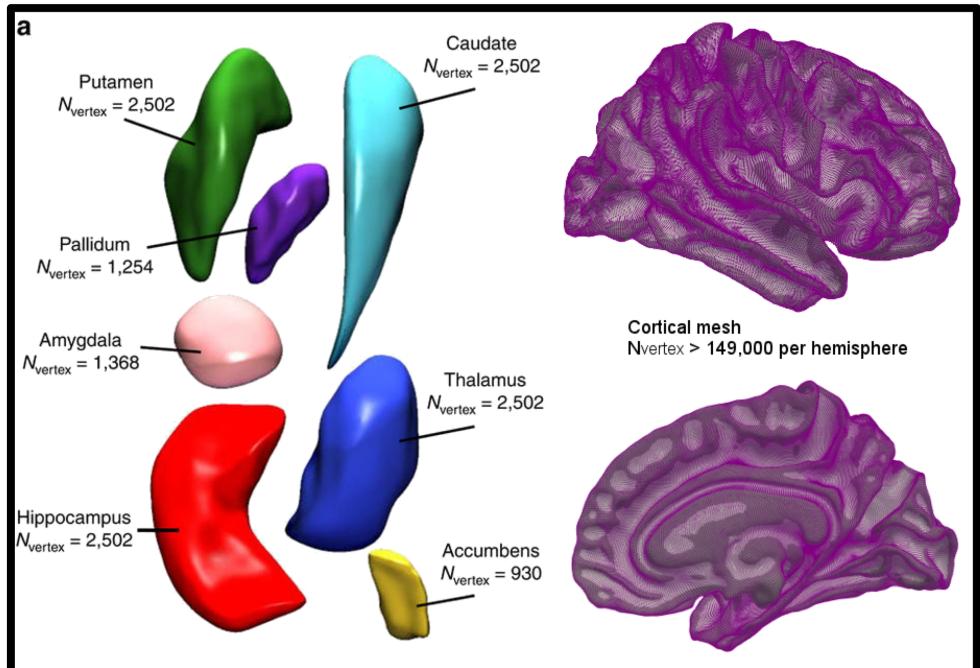


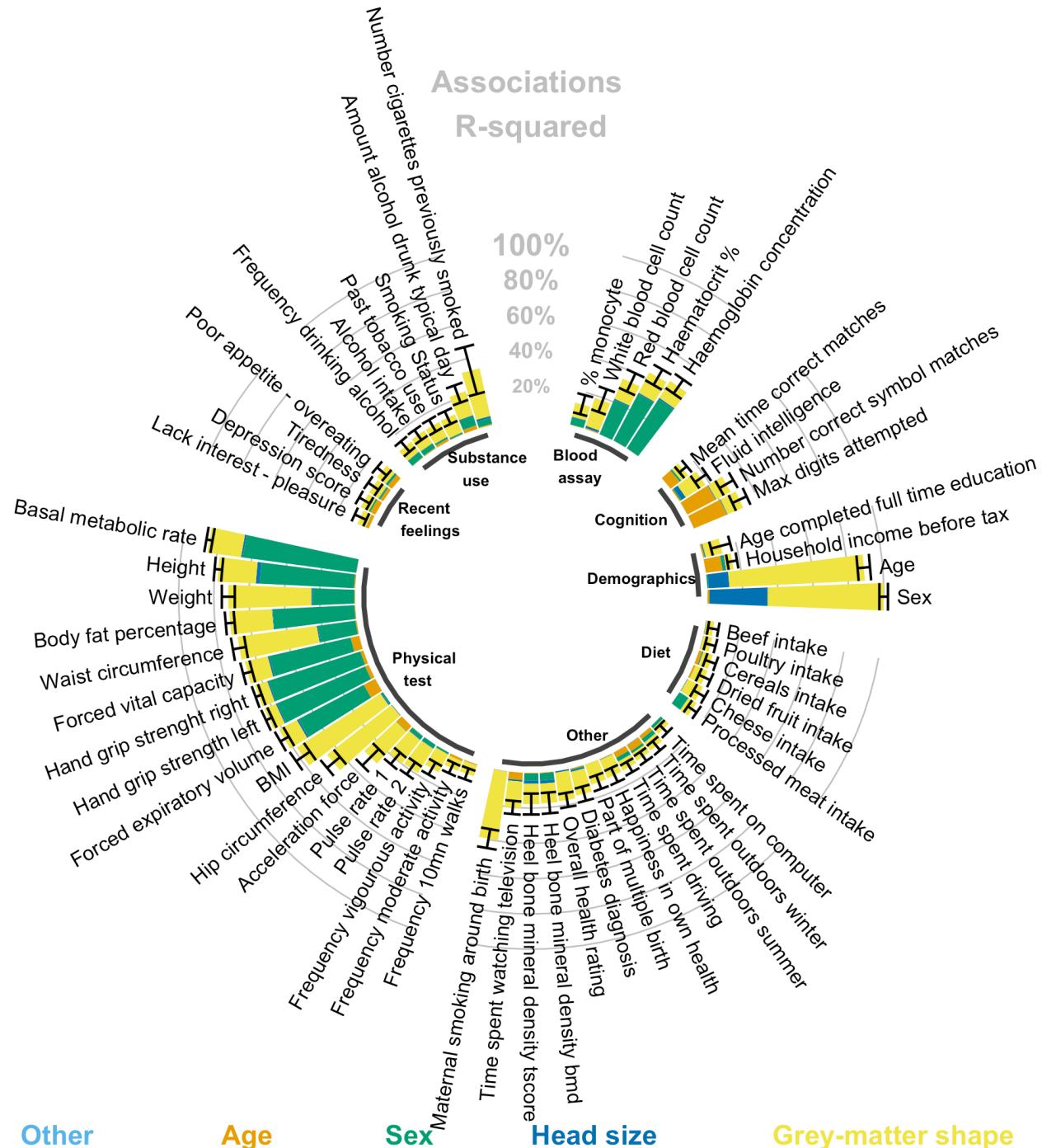
Figure
adapted
from
Roshchupkin
Et al. 2016

Brain-morphometricity

UK Biobank discovery sample (N=9,888)

58/175 significant associations

- Demographics (age, sex, education, income level)
- Body size, physical measurements, strength
- Cognition
- Alcohol & tobacco use
- Maternal smoking around birth
- Lifestyle, self-rating
- Diabetes
- Blood assay results
- Diet
- Depression scores and symptoms

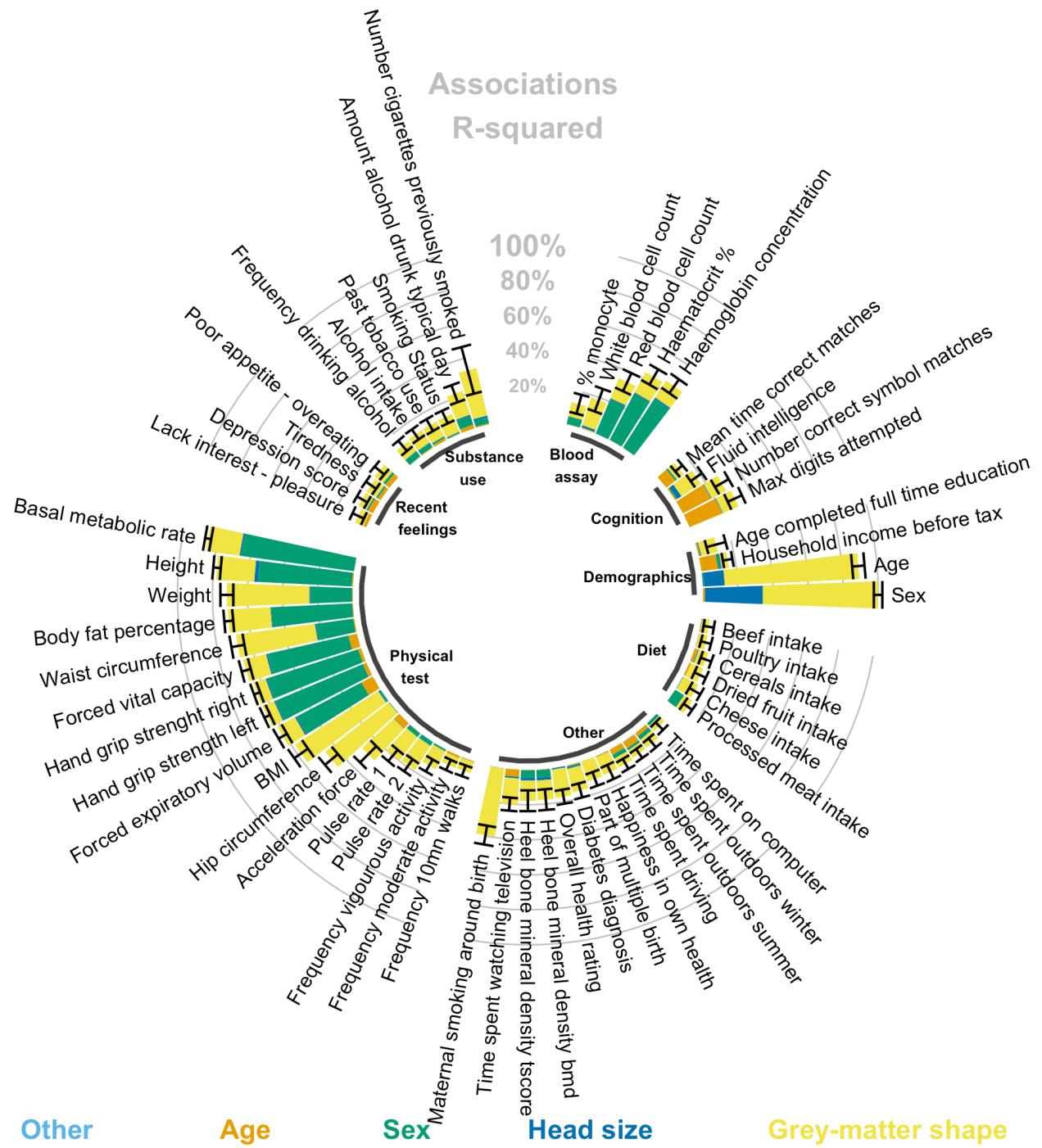
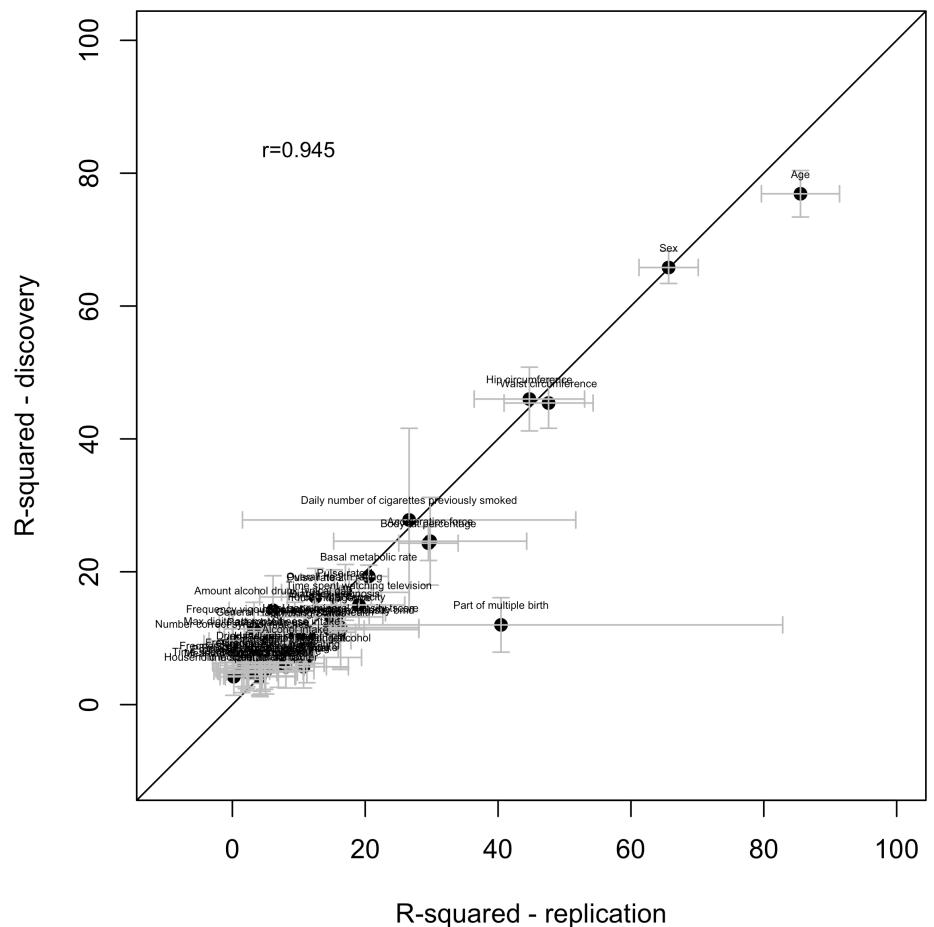


Brain-morphometric replication

UK Biobank discovery sample: N=9,888

UK Biobank replication sample: N=4,323

23/58 associations replicated



Grey-matter correlations

Shared brain-morphometricity between traits

May reflect, causal, bi-directional confounded relationships

A lot of the brain-morphometricity detected is common to that of body size (height, weight, BMI, waist and hip circumference)

=> In particular: depression scores, diet, blood assay, activity levels



Phenotype prediction

Grey-matter scores significantly predict

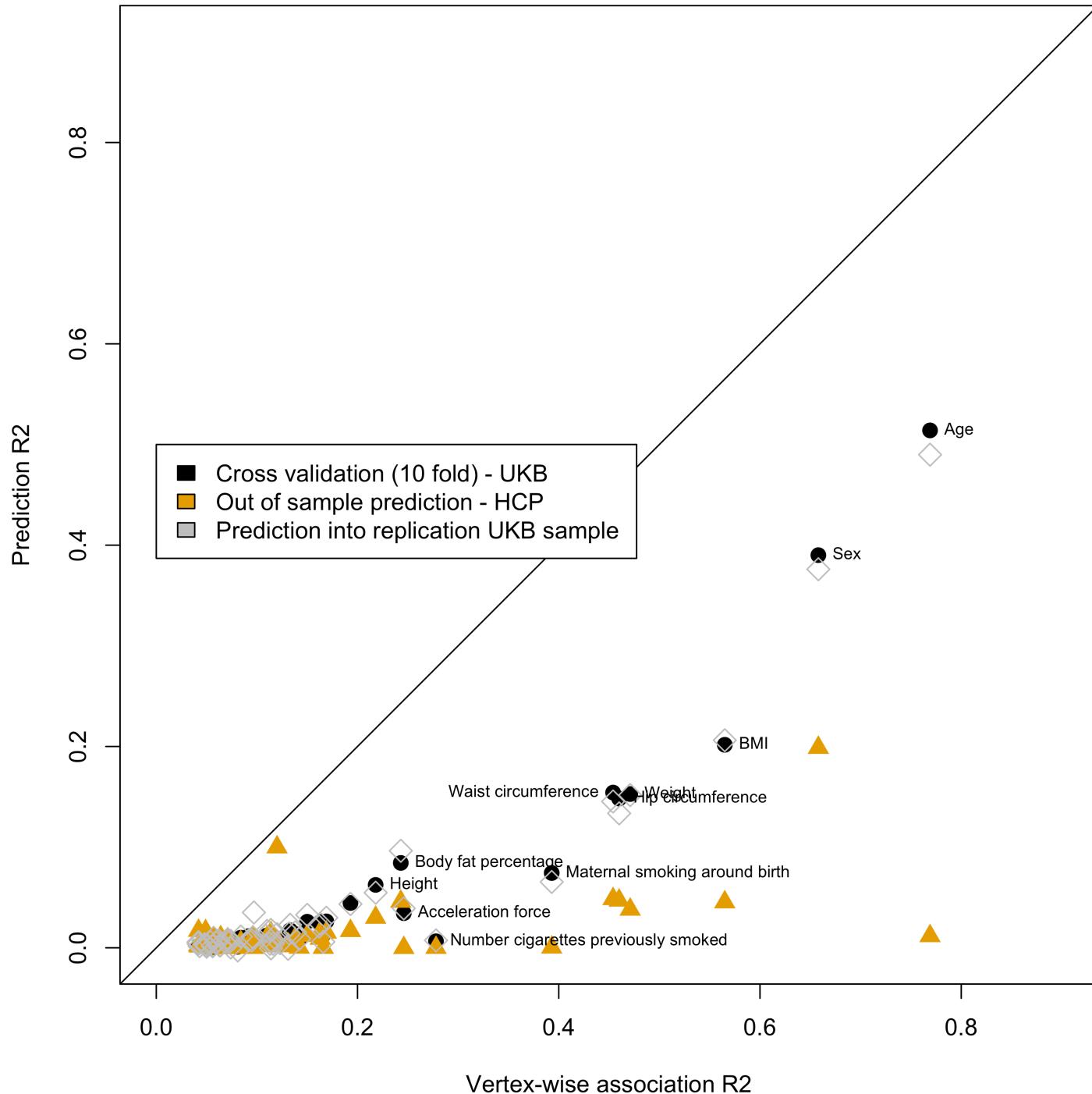
- **56/58 phenotypes in 10-fold cross validation**
- **42 phenotypes in the UKB replication sample**
- **19 HCP phenotypes**

The shared morphometricity between depression score and body size may be leveraged in prediction

- Depression score best predicted ($r=0.1$) from grey-matter score of BMI

Application to new samples

- Grey-matter score for maternal smoking around birth correlates with nicotine dependence (FNTD) in the HCP
- Active and passive smoking?



Thank you to all UK Biobank participants and staff

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Jian Yang

Peter Visscher

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Lachlan Strike

Margaret Wright

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Olivier Colliot



Program for Complex Trait Genomics (PCTG)