Linking brain phenotypes with cardiovascular risk factors through GWAS

Brain image-derived phenotypes (IDPs)

White Matter Hyperintensity (WMH):

- total volume (T2 FLAIR)
- lesion count

QSM and T2* applied on WMH

QSM for (left and right):

- Caudate
- Putamen
- Pallidum
- Substantia Nigra
- Amygdala

Iron quantification in different areas

Cardiovascular risk factors and diseases

- **Hypertension**
- **Diastolic blood pressure**
- **Systolic blood pressure**
- **Glucose**
- **Diabetes**
- **HDL**
- **LDL**
- **Triglycerides**
- **Body mass index (BMI)**
- *Coffee intake*
- *Current tobacco smoking*
- *Sleep duration*
- *Alcohol intake frequency*
- *Time spent doing moderate physical activity*
- **Stroke**

More environmental variables

Data used

2017 UKBioBank GWAS round 2 by Neale lab

- ❑https://github.com/Nealelab/UK_Biobank_GWAS
- ❑UKBB GWAS Imputed v3 - File Manifest Release 20180731 - Google Sheets

Brain phenotypes:

- BIG40 (2020) for all except WMH lesion count

- ❑https://www.fmrib.ox.ac.uk/ukbiobank/gwas_resources/index.html
- ❑https://open.win.ox.ac.uk/ukbiobank/big40/

But why these phenotypes?

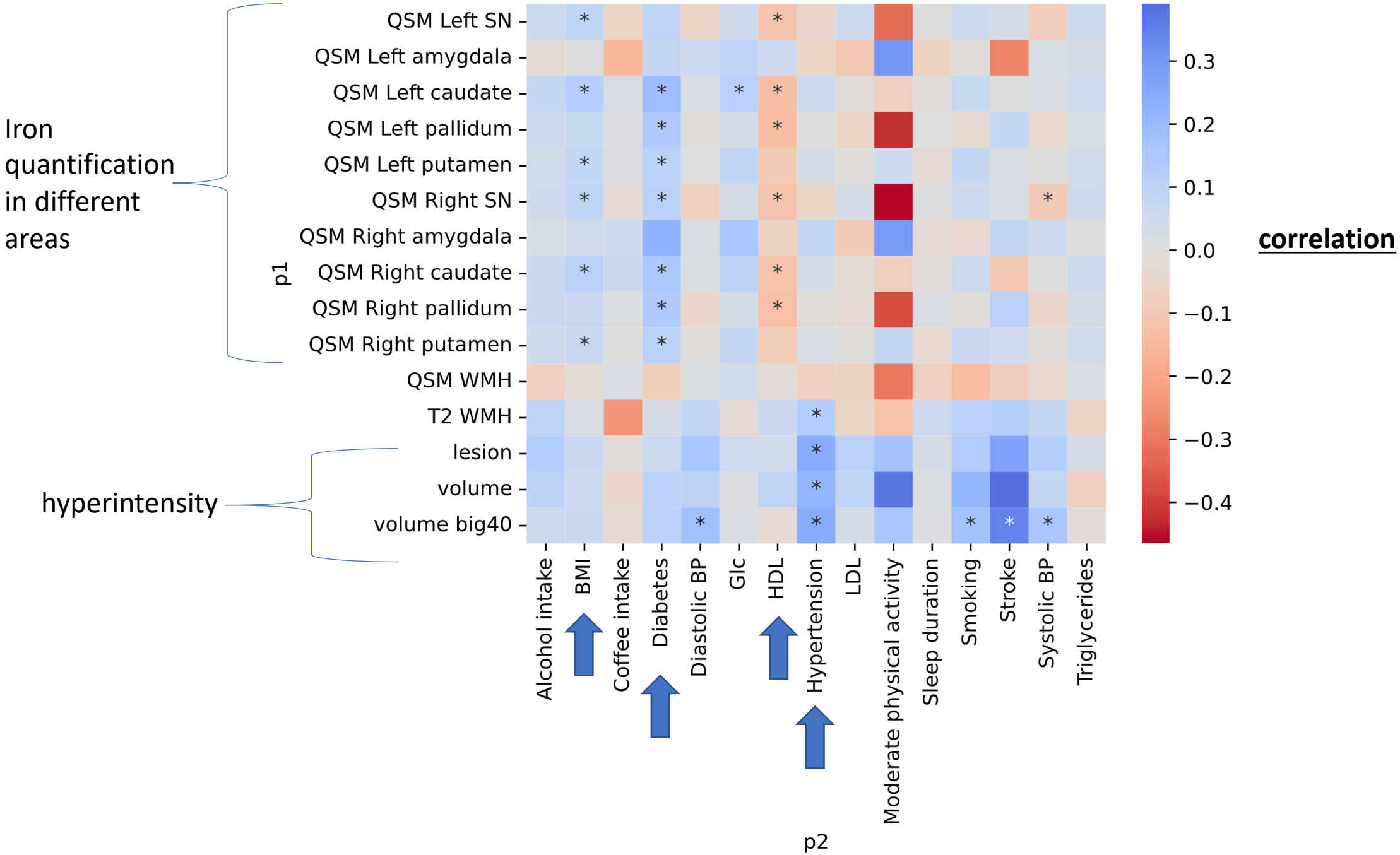
- Chosen based on significant **phenotypic correlations** found in other studies
  - Mainly based on results by:
    - Wang, C., Martins-Bach, A.B., Alfaro-Almagro, F. *et al.* Phenotypic and genetic associations of quantitative magnetic susceptibility in UK Biobank brain imaging. *Nat Neurosci* **25**, 818–831 (2022).

Question: are these correlations only due to environmental **confounders** or can we find **genetic** correlations as well?

1. Estimating genetic correlation

with linkage disequilibrium score regression

ldsc


Iron quantification in different areas
hyperintensity
QSM Left SN
QSM Left amygdala
QSM Left caudate
QSM Left pallidum
QSM Left putamen
QSM Right SN
QSM Right amygdala
QSM Right caudate
QSM Right pallidum
QSM Right putamen
QSM WMH
T2 WMH
lesion
volume
volume big40
p1
Alcohol intake
BMI
Coffee intake
Diabetes
Diastolic BP
Glc
HDL
Hypertension
LDL
Moderate physical activity
Sleep duration
Smoking
Stroke
Systolic BP
Triglycerides
p2
0.3
0.2
0.1
0.0
−0.1
−0.2
−0.3
−0.4
correlation

2. Cross-GWAS coherence test

PascalX

(results are pending…)

See more about methods and results

https://github.com/peruginiandrea/scripts