Aggression in Children: Unraveling gene-environment interplay to inform Treatment and InterventiON strategies

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The research leading to these results has received funding from the European Union Seventh Framework Programme (FP7/2007-2013) under grant agreement no 602768

Genome-wide Heritability of Metabolomics-derived Blood Metabolites

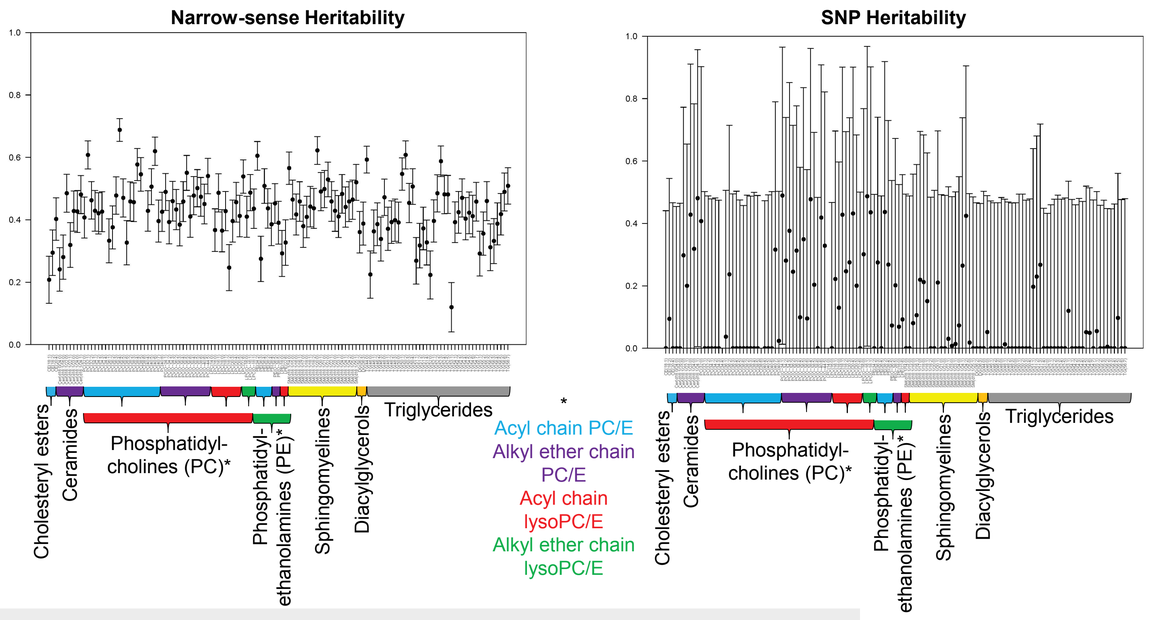
F.A. Hagenbeek[1,2], M.G. Nivard[1], R. Pool[1,2,3], H.H.M. Draisma[4], JJ. Hottenga[1,5] G. Willemsen[1,2], A. Abellaoui[1], A. Harms[6,7], BBMRI-NL[3], T. Hankemeier[6,7], M. Bartels[1,2,5] & D.I. Boomsma[1,2,5]

[1]Department of Biological Psychology, VU Amsterdam, Amsterdam, the Netherlands. [2]EMGO+ Institute for Health and Care Research, Amsterdam, the Netherlands. [3]BBMRINL: Infrastructure for the Application of Metabolomics Technology in Epidemiology, Leiden, The Netherlands. [4]Department of Human Genetics, Leiden University Medical Center, Leiden, The Netherlands. [5]Neuroscience Campus Amsterdam, Amsterdam, the Netherlands. [6]Division of Analytical Biosciences, Leiden Academic Center for Drug Research, Leiden University, Leiden, The Netherlands. [7]The Netherlands Metabolomics Centre, Leiden, The Netherlands.

Introduction

- Metabolomics twin and family studies report medium-to-high heritability (h^2) estimates (e.g., Kettunen et al. 2012; Draisma et al. 2013; Shin et al. 2014).
- Metabolomics GWAS report associations with explained variances which can exceed 10% (Kastenmüller et al. 2015).
- Previously, Rhee et al. (2016) investigated the contribution of common & rare variants to overall SNP h^2.
  - **Aim:** Estimate both narrow-sense & SNP h^2 for 4 metabolomics platforms measured in NTR blood samples.

Fig. 2: Lipidomics heritability estimates



Results

- Narrow-sense and SNP h^2 for each of the platforms in **Fig.1-4**.
- Comparison with Rhee et al. in **Fig.5.**
  - 78/94 metabolites fall within C.I. of Rhee et al. estimates.

Fig. 3: LUMC heritability estimates

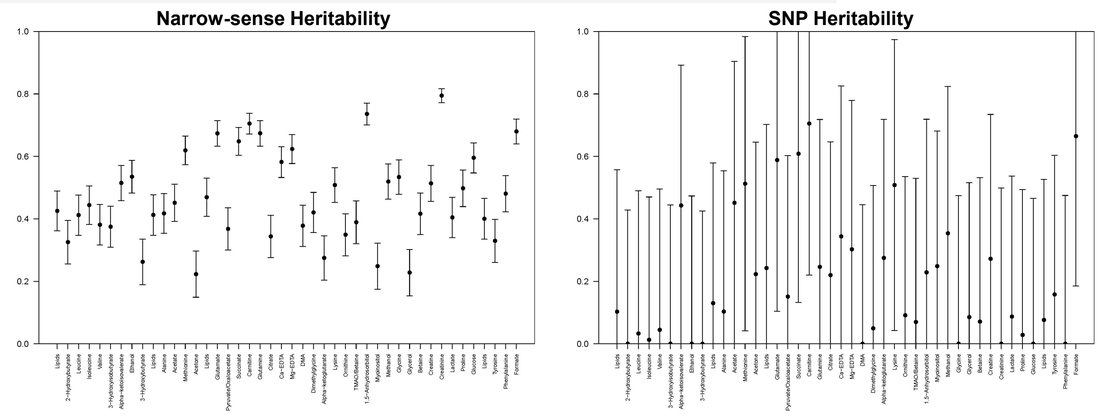


Fig. 4: Brainshake heritability estimates

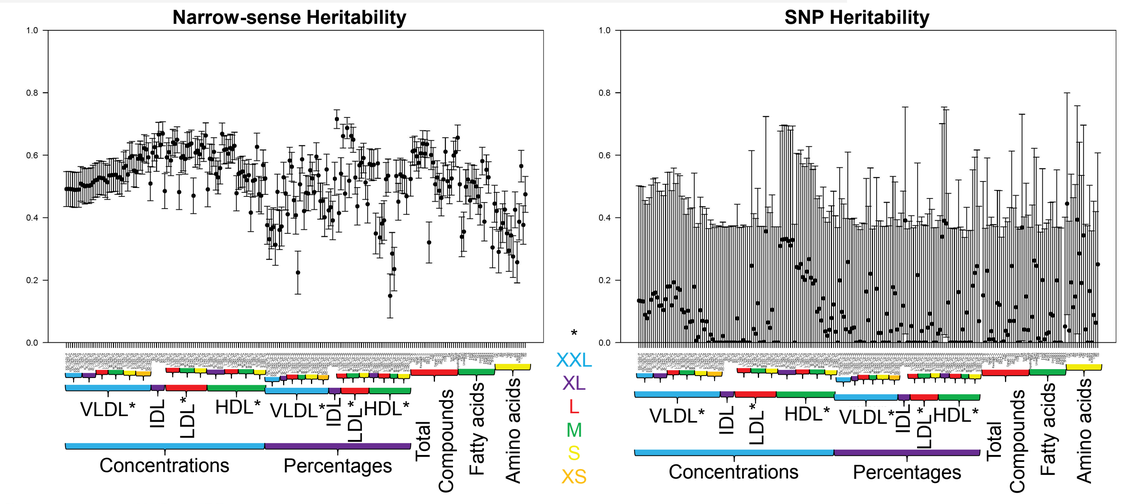
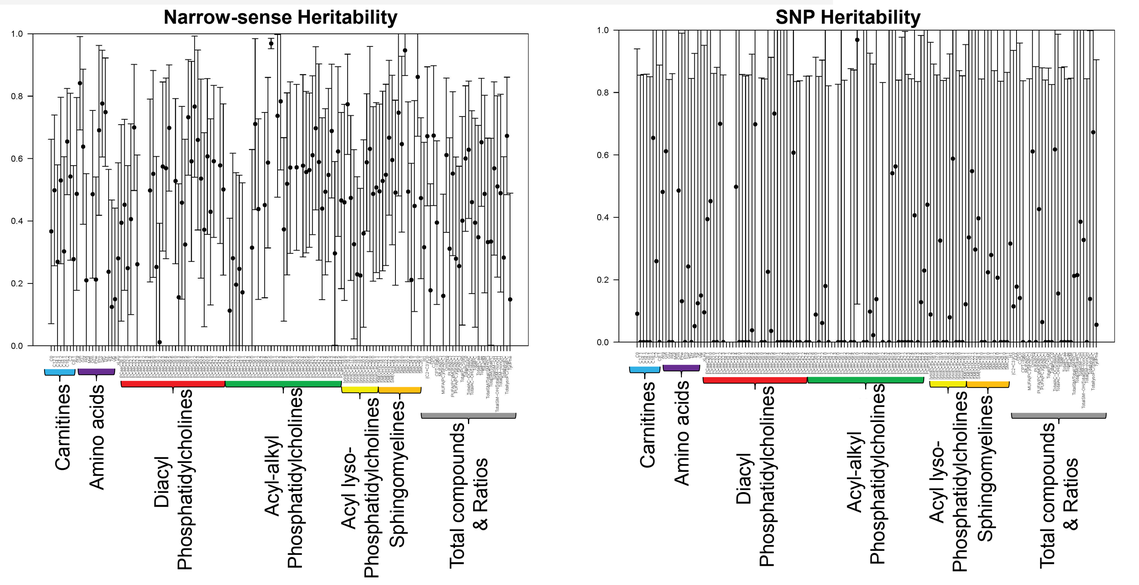


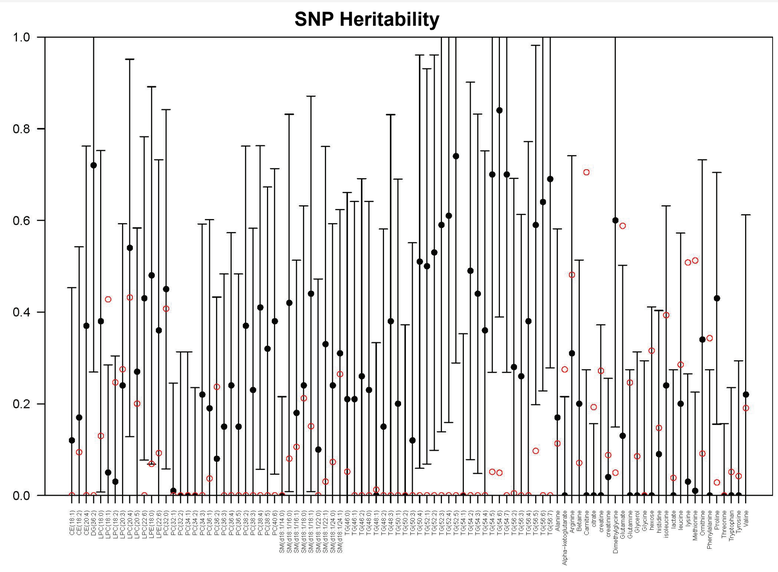
Fig. 1: Biocrates heritability estimates



Methods & statistics

- **Participants**: selection of twins and family members of NTR participating in Biobank Project.
- **Samples**: fasting blood samples.
- **MS Platforms:** Biocrates [*N*~1,077; *M*=145] & Lipidomics [*N*~2,248; *M*=131].
- **NMR platforms:** LUMC [*N*~2,320; *M*=44] & Brainshake [*N*~2,890; *M*=225].
- **Genetic data:** 1,261,818 SNPs & *N* = 15,110 → no ethnic outliers, autosomes only, HWE > $1x10^{-5}$, MAF > 0.01.
- **GRM:** Down-weighting of high-LD SNPs in GRM construction (*LDAK*; Speed et al. 2012).
- **Statistics:** Simultaneous estimation of narrow-sense & SNP h^2 by including two GRMs in *GCTA* (Yang et al. 2010; Yang et al. 2011).
  - 1) 'full' GRM with both closely & distantly related pairs of individuals
  - 2) 'family' GRM with values of distantly related pairs of individuals set to zero (Zaitlen et al. 2013).

Fig. 5: Comparison with Rhee et al.



- SNP heritability estimates as reported by Rhee et al. (2016)
- SNP heritability estimates as found in current study

Conclusions

- Narrow-sense heritability estimates similar to those obtained in classic twin-family studies of similar platforms.
- Direct comparison with previous SNP h^2 difficult as both studies are underpowered and use different platforms and GRMs.
- Congruent with Rhee et al. (2016), common SNPs alone are not sufficient to explain variation for all metabolites levels.

Contact: f.a.hagenbeek@vu.nl