Patterns of Genetic Influence on Variation in High-Dimensional Metabolomics Data

F.A. Hagenbeek1, H.H.M. Draisma1,2,3, A. Harms4,5, M. Bartels1,2, T. Hankemeier4,5 & D.I. Boomsma1,2,3

1Department of Biological Psychology, VU Amsterdam, Amsterdam, the Netherlands. 2EMGO+ Institute for Health and Care Research, Amsterdam, the Netherlands. 3Neuroscience Campus Amsterdam, Amsterdam, the Netherlands. 4Leiden Academic Center for Drug Research, Division of Analytical Biosciences, Leiden University, Leiden, the Netherlands. 5The Netherlands Metabolomics Centre, Leiden, the Netherlands

Heritability estimates for LC-MS blood plasma lipids under AE model

Results

> Twin correlations indicated genetic model including "common environment" in majority of lipids (Figure 1)
> ACE genetic model acceptable for 102 of 131 lipids → AE submodel best fit for 118 of 131 lipids
> Lipid heritability (H2) was low-moderate (≤60%) under AE-model (Figure 2)
> H2 triglycerides (TGs) seems to depend on number of carbon atoms & double bonds in fatty acid chain

Discussion & Conclusions

> Approximately half of individual differences in blood plasma lipids are accounted for by genetic differences
> Pattern of genetic influence in TGs previously observed6 & for phosphatidylcholines4
> Patterns could reflect metabolic conversions rounds in anabolism & catabolism or use of different acyl-CoA dehydrogenase isozymes in β-oxidation
> Number of TG carbon atoms & double bonds associated with disease risk11, H2 could reflect this

Future directions

> SNP and narrow-sense heritability for all adult NTR metabolomics datasets

Materials & Methods

> 2543 NTR7 Biobank project8 twins with blood plasma available – 1387 monozygotic (MZ) & 1126 dizygotic (DZ) twins
> 131 blood plasma lipids from 9 different biochemical classes via liquid chromatography mass spectrometry (LC-MS)
> Twin correlations in R
> Heritability estimates via genetic analysis using structural equation modelling in OpenMx software9

Introduction

> Metabolomics: comprehensive analysis of low-molecular weight compounds in biological samples1
> Lipidomics: subfield with focus on lipids (e.g., glycerolipids, sphingolipids, etc.)
> Metabolites are biological endophenotypes; reflect genetic & environmental influences1,2
> Genetic studies into the metabolome have been reported3,4 – included lipids6 – no lipodomics heritability estimates
> Current study: heritability of lipids delivered by targeted LC-MS in adult twin sample

Figure 1. Twin correlations for LC-MS blood plasma lipids.

The dots indicate the point estimate for the twin correlations, the whiskers are the maximum likelihood based 95%-confidence intervals for these point estimates. Lipids are ordered by an increasing number of carbon atoms and double bonds in their side chains for each of the lipid classes.

Figure 2. Heritability estimates for LC-MS blood plasma lipids under AE model

The dots indicate the point estimate for the standardized A variance component, the whiskers are the maximum likelihood based 95%-confidence intervals for these point estimates. Lipids are ordered by an increasing number of carbon atoms and double bonds in their side chains for each of the lipid classes.

References