ACTION

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

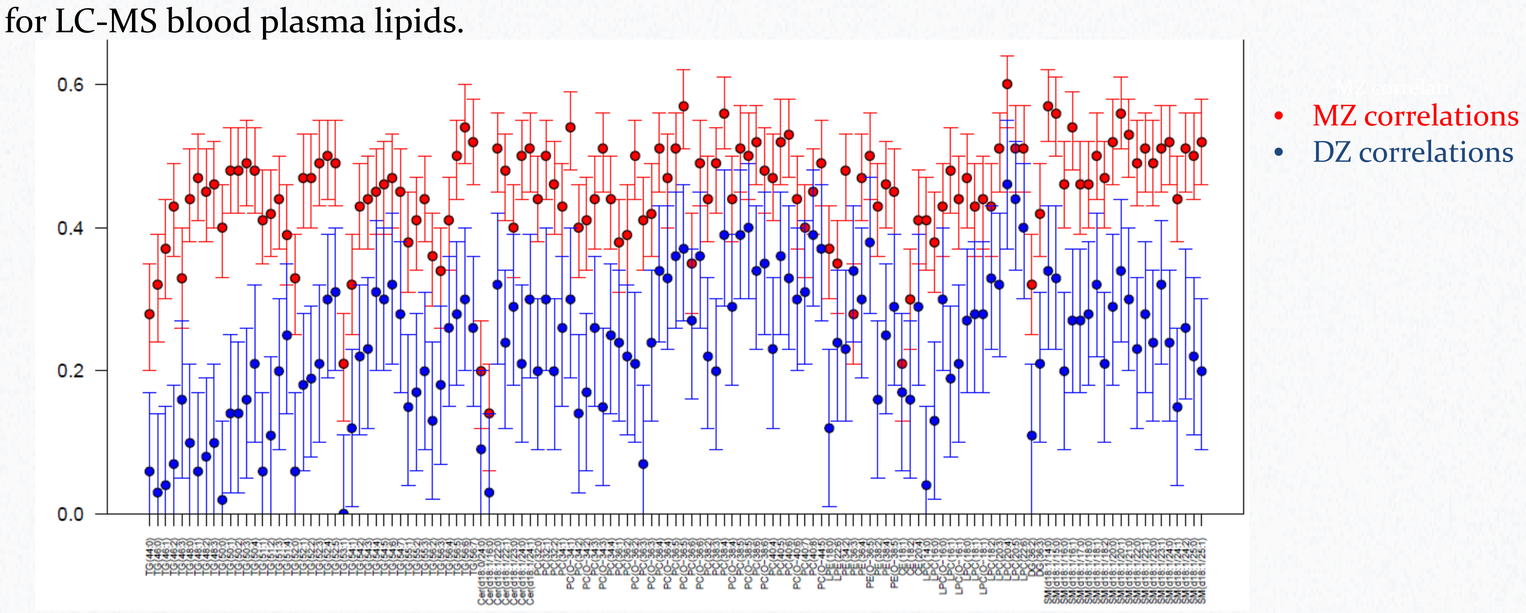
Patterns of Genetic Influence on Variation in High-Dimensional Metabolomics Data

F.A. Hagenbeek[1], H.H.M. Draisma[1,2,3], A. Harms[4,5], M. Bartels[1,2], T. Hankemeier[4,5] & D.I. Boomsma[1,2,3]

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

Contact: f.a.hagenbeek@vu.nl http://www.action-euproject.eu

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.

Introduction

- Metabolomics: comprehensive analysis of low-molecular weight compounds in biological samples[1]
- Lipidomics: subfield with focus on lipids (e.g., glycerolipids, sphingolipids, etc.)
- Metabolites are biological endophenotypes; reflect genetic & environmental influences[1,2]
- Genetic studies into the metabolome have been reported [e.g., 3,4,5] → included lipids[6] → no lipidomics heritability estimates
- Current study: heritability of lipidomics derived lipids by targeted LC-MS in adult twin sample

Materials & Methods

- 2543 NTR[7] Biobank project[8] 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 software[9]

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 sub-model best fit for 118 of 131 lipids
- Lipid heritability (H^2) was low-moderate (<60%) under AE-model (**Figure 2**)
- H^2 triglycerides (TGs) seems to depend on number of carbon atoms & double bonds in fatty acid chain

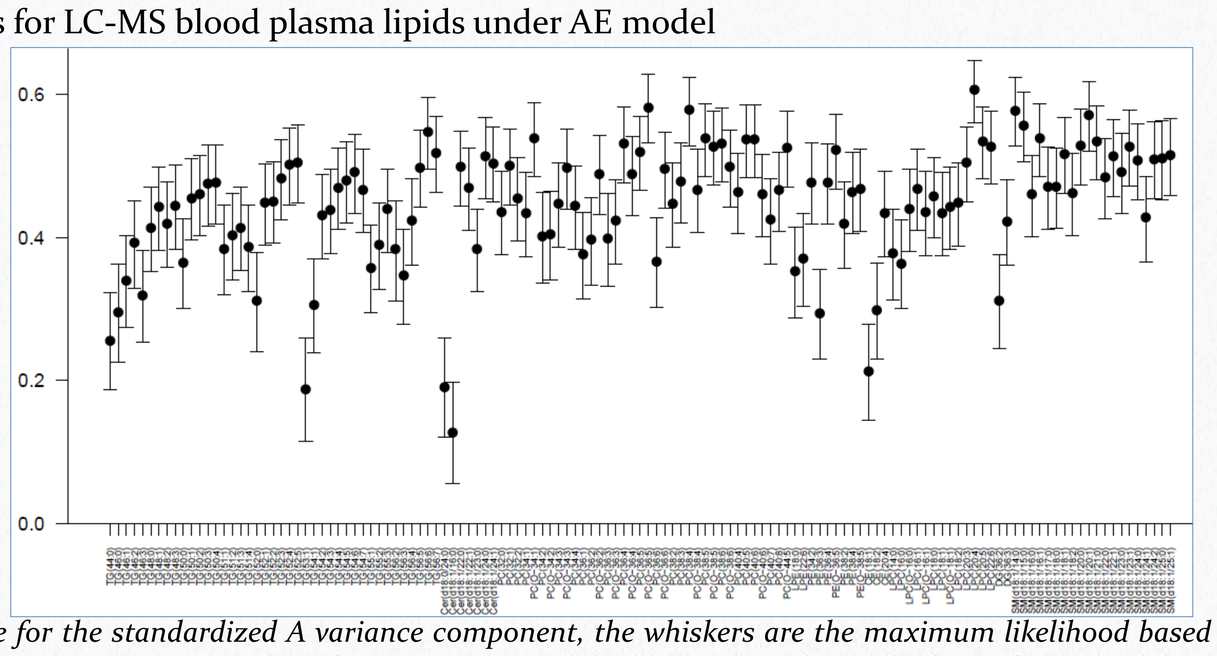
Discussion & Conclusions

- Approximately half of individual differences in blood plasma lipids are accounted for by genetic differences
- Pattern of genetic influence in TGs previously observed[10] & for phosphatidylcholines[4]
- 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 risk[11], H^2 could reflect this

Future directions

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

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.

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