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GWAS, EWAS, and metabolomics of longitudinal aggression and attention problems

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Introduction

Twin studies have been at the forefront in leveraging the analyses of multivariate and longitudinal data, but GWA studies have so far made limited use of these approaches. The analysis of multiple measures in GWA studies is non-trivial as repeatedly including the same subject in meta-analysis inflates type-1 error. The ACTION consortium is, in collaboration with other child cohorts, carrying out a GWAMA of the (developmental) genetic etiology of Aggression (AGG) and Attention problems (ATT), an EWAS and a biomarker study (metabolomics).

GWAM Approach

- A total of 29 cohorts are now included in the meta-analyses of childhood aggression / attention problems
- We include multiple raters: mother, father, teacher, self and also retrospective ratings
- We currently have 277,197 observations for the AGG GWAMA. The ADHD GWAMA has 241,685 observations.
- In summary, we obtained GWAS summary statistics for: Aggressive behavior & ADHD-symptoms
  - Repeatedly measured between ages 2 - 18
  - 5 raters (mother, father, self, teacher, retrospective)
  - 10 instruments
  - 1 - 52 GWA per cohort (238 GWAs in total)

Metabolomics

Number of twins from concordant and discordant (MZ) twin pairs with DNA collection & urine collected for metabolomics (in addition, a sample of 189 children from child psychiatry clinics will be included).

In total 20 cohorts, N=15215; mainly whole blood.


Next steps

- Finalize Meta-analysis of all cohorts, for Aggression and Attention Problems
- Analysis of age-, rater- and instrument- specific associations
- PRS and gene-environment correlation analyses
- Finalize meta-analysis of epigenetic data for Aggression
- Present results at ACTION final meeting

The ACTION final meeting on aggression studies will take place in Sardinia, Italy in 2019 (May 6-8, Hotel Flamingo, Santa Margherita di Pula). Registration forms for the hotel reservation and for the science meeting are available from the Action webpage (http://www.action-euproject.eu/events)

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