

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

Dorret I. Boomsma, Meike Bartels, Jenny van Dongen, Michel Nivard, Hill Ip, Fiona Hagenbeek, Peter Roetman on behalf of the ACTION consortium

Dept Biological Psychology, VU Amsterdam, Amsterdam, the Netherlands / Leiden Univ Medical Centre, Leiden, the Netherlands

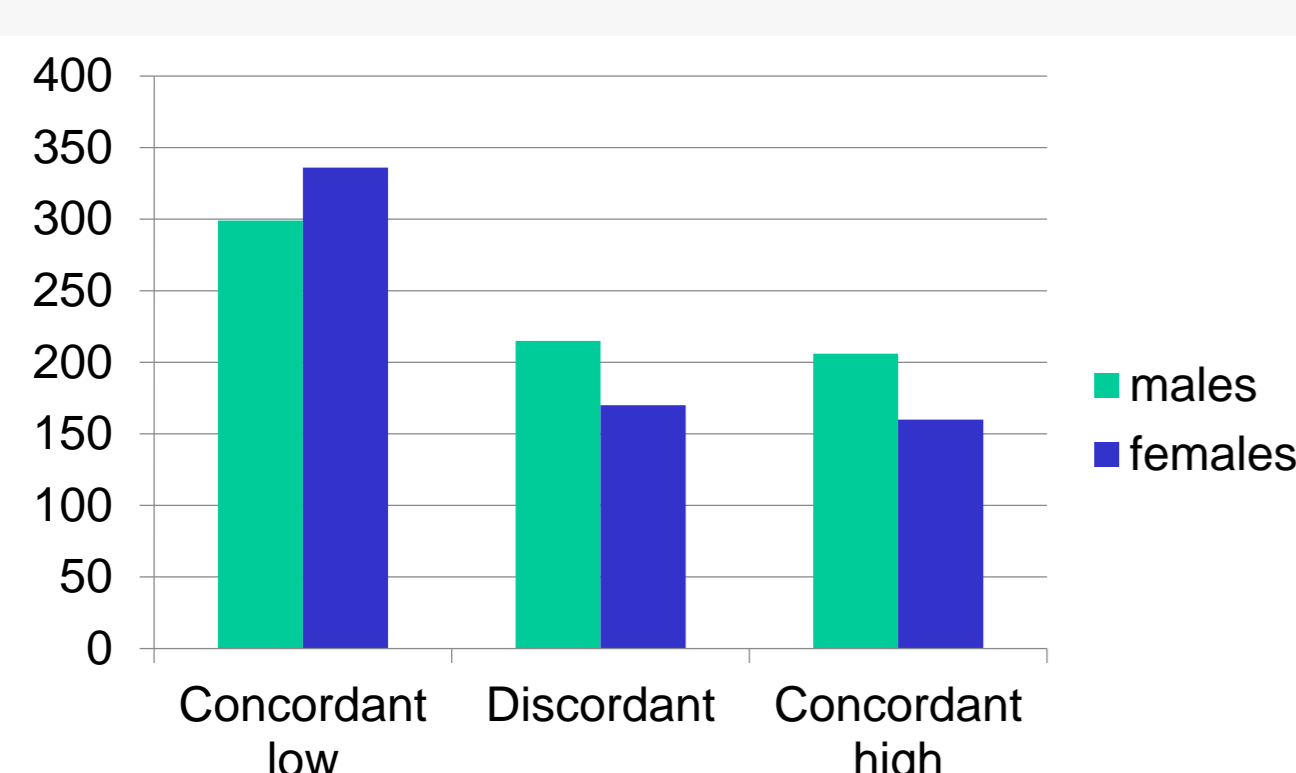
### Introduction

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

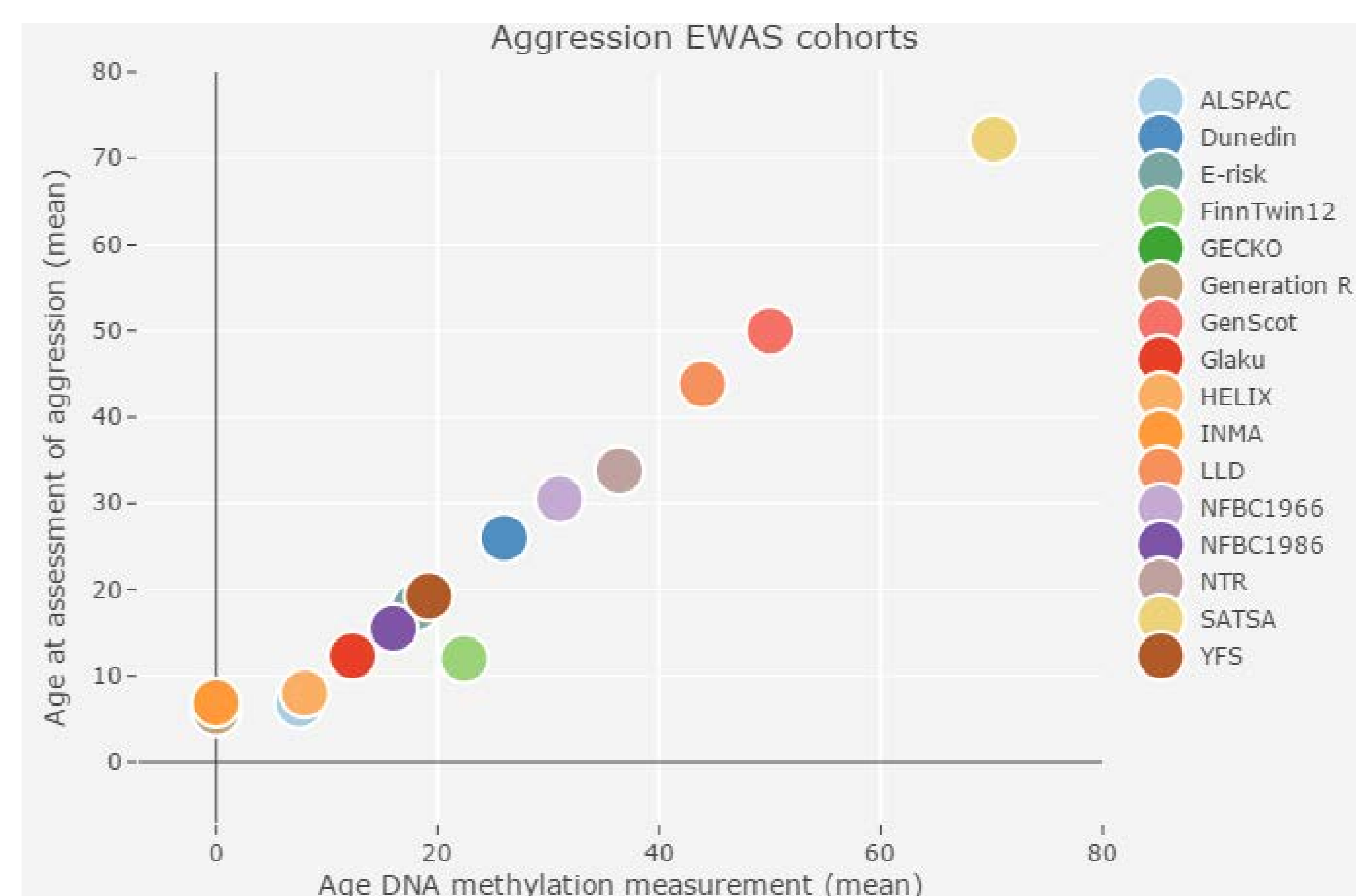
- **A total of 29 cohorts** are now included in the meta-analyses of childhood aggression / attention problems
- We include **multiple raters**: mother, father, teacher, self and also retrospective ratings
- We currently have **277,197 observations for the AGG GWAMA**. The **ADHD GWAMA has 241,685 observations**.
- 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).

### Fig 1: EWAS meta-analysis for aggression



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

EWAS for Attention Problems (N= 4689). : Van Dongen et al. in press, Biol Psychiatry).

### 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>)

