ACTION

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

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Polygenic score prediction of insomnia on childhood aggressive behaviour in the Netherlands Twin Register

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Introduction

- Insomnia = difficulty falling asleep, difficulty staying asleep & waking earlier than intended
- Insomnia has been associated with anger, irritability, aggression and conduct problems across the lifespan.

- **Hypothesis:** the genetic liability for insomnia predicts aggressive behaviour across the lifespan.
  - Here, we focus on the prediction of childhood aggression

Table 1 – cohort description

|	N (N families)	Age Mean (sd) [range]	Sex N (%)	Aggression Mean (sd) [range]
CBCL age 3	4,705 (2,520)	3.3 (0.3) [2.8 – 4.9]	Boys: 2,232 (47.4%) Girls: 2,473 (52.6%)	10.4 (6.7) [0 – 36]
CBCL age 7	4,032 (2,164)	7.5 (0.4) [6.8 – 9.7]	Boys: 1,913 (47.4) Girls: 2,119 (52.6%)	5.1 (5.1) [0 – 34]
CBCL age 10	4,455 (2,384)	9.9 (0.5) [7.8 – 11.9]	Boys: 2,086 (46.8%) Girls: 2,369 (53.2%)	4.4 (4.8) [0 – 33]
CBCL age 12	2,976 (1,608)	12.2 (0.4) [11.1 – 13.7]	Boys: 1,351 (45.4%) Girls: 1,625 (54.6%)	3.9 (4.4) [0 – 31]

Results

- No significant prediction of childhood aggression from insomnia PGS (**Table 2; Figure 1**).

Table 2 – gee + meta-analysis results

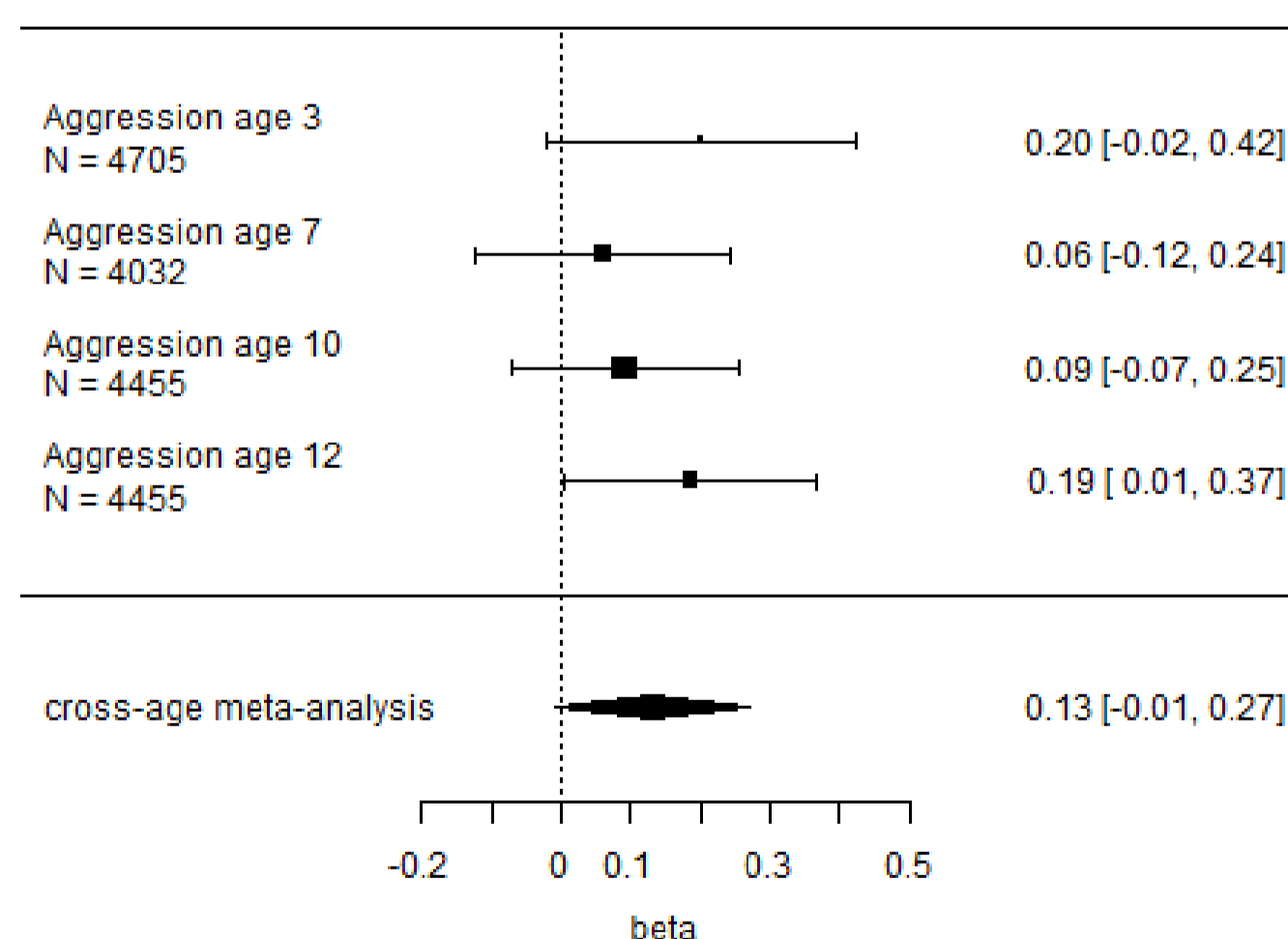|	Beta	Robust SE	P-value	R^2
CBCL age 3	0.20	0.11	0.07	0.0404
CBCL age 7	0.06	0.09	0.52	0.0037
CBCL age 10	0.09	0.08	0.26	0.0086
CBCL age 12	0.19	0.09	0.04	0.0345
Cross-age meta-analysis	0.13	0.07	0.07	0.0173

Methods

Hammerschlag et al. (2017)
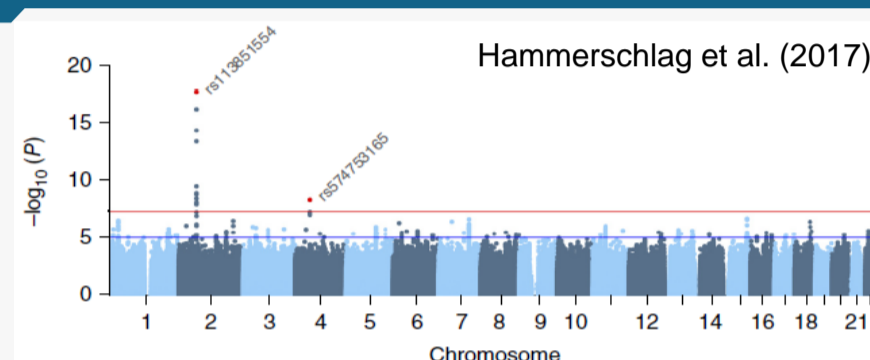
3 loci for insomnia reported for 113,006 individuals of European descent in the UK Biobank study. Cases = 32,384; Controls = 80,622

- **Polygenic scores (PGS):** PGS based on adult insomnia (Hammerschlag et al. 2017).
- **Childhood aggression:** aggression scale from the Child Behavior Checklist (CBCL) for Dutch twins at age 3, 7 ,10 and 12. → cohort description **Table 1**.
- **Statistical analyses:**
  - GEE with sandwich-correction to correct for relatedness in R
    - Aggression ~ Insomnia PGS + sex + age + age^2 + sex*age + sex*age^2 + PC1-PC10 + genotyping chip
  - Cross-age meta-analysis in metafor (R)

Figure 1 – forest plot

Aggression age 3 N = 4705 — 0.20 [-0.02, 0.42]
Aggression age 7 N = 4032 — 0.06 [-0.12, 0.24]
Aggression age 10 N = 4455 — 0.09 [-0.07, 0.25]
Aggression age 12 N = 4455 — 0.19 [0.01, 0.37]
cross-age meta-analysis — 0.13 [-0.01, 0.27]

Conclusions & Future directives

- The genetic liability for insomnia was not significantly associated with childhood aggressive behavior at specific ages or in the cross-age meta-analysis.

- Further analyses will investigate whether the insomnia PRS does predict aggression in adolescents or adults in NTR.
- Once available, update NTR analyses with GWA summary statistics from Jansen et al. (*in press*) which identified 202 loci for insomnia.
- Finally, insomnia PGS prediction for aggressive behavior will be meta-analyzed across multiple cohorts (**R. Lavender, L. Colodro Conde & S. Medland**)

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