

Genome-wide association meta-analysis of expressive and receptive vocabulary from infancy to early childhood

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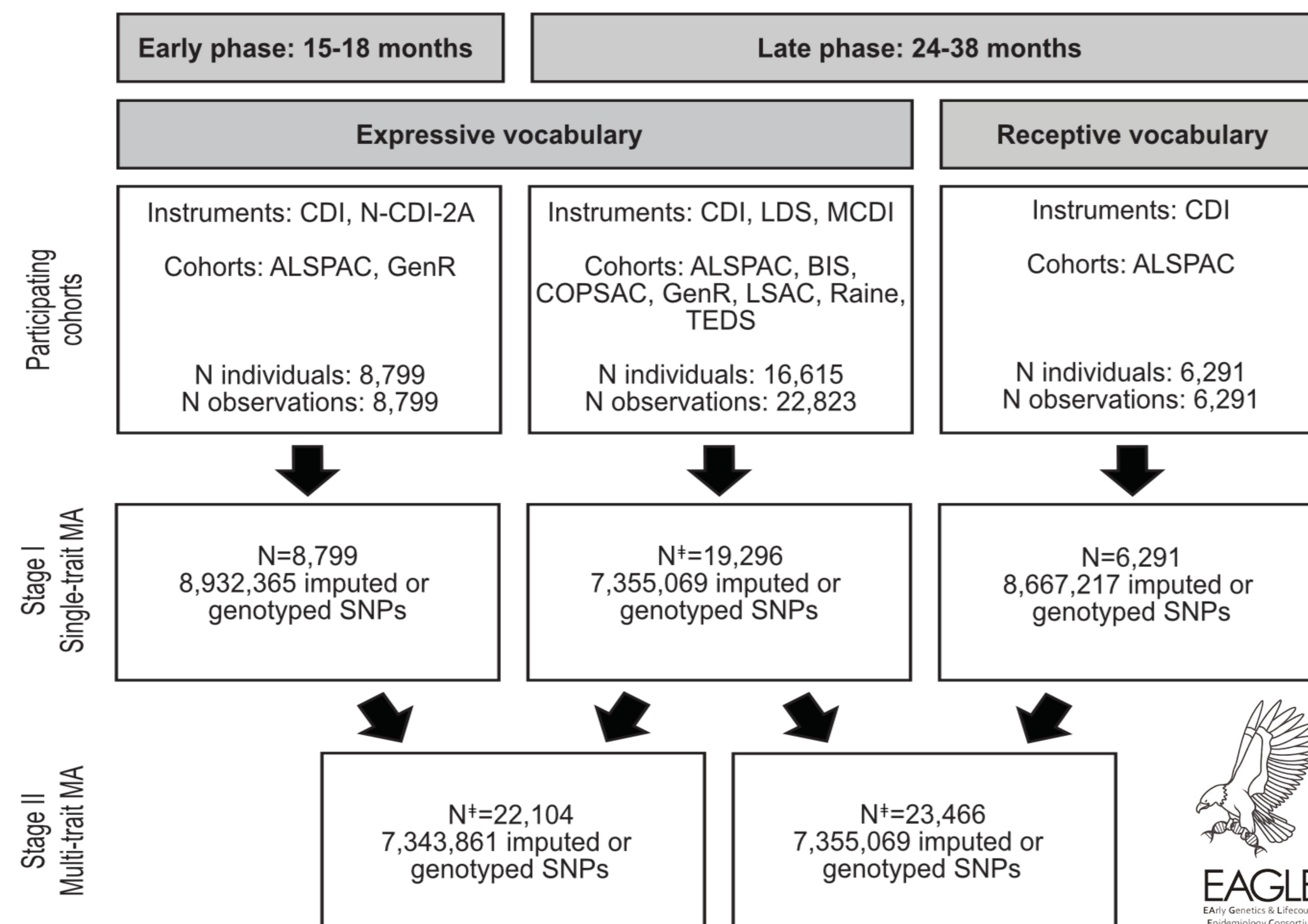
In a nutshell - we aimed to ...

(i) identify genome-wide association signals for early vocabulary, (ii) elucidate the underlying genetic architecture and (iii) characterise polygenic links with later-life cognitive, behavioral and health outcomes.

Background

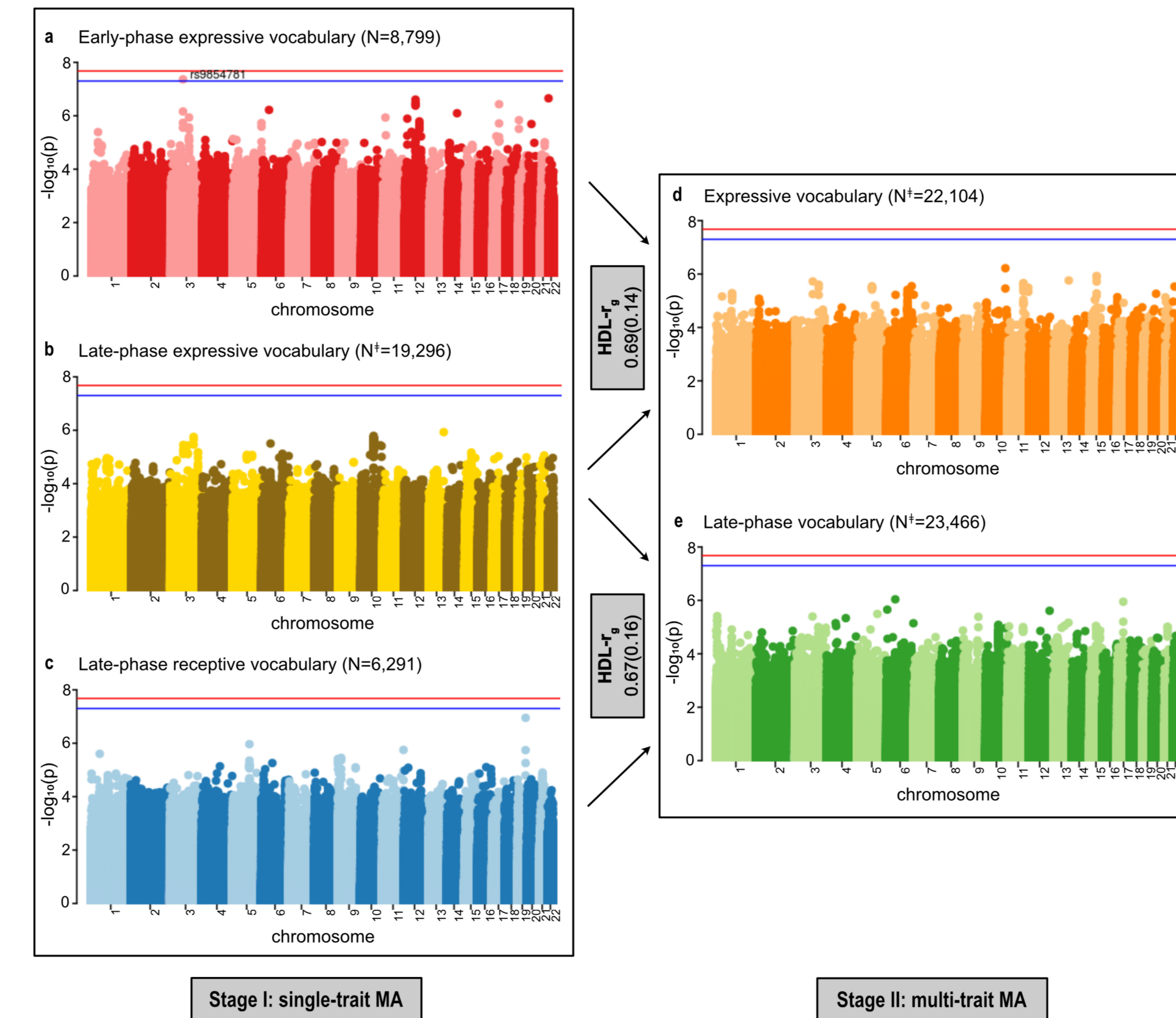
The genetic architectures underlying expressive and receptive vocabulary in early life are complex and little characterised. Here, we present the largest meta-genome-wide association study (meta-GWAS) of early vocabulary (15-38 months) till date, based on 37,913 observations and 17,298 individuals, within the Early Genetics and Life Course Epidemiology (EAGLE) Consortium.

Study design



Expressive and/or receptive vocabulary was assessed using parent questionnaires in children of European descent from seven independent population-based or community-based cohorts. Meta-GWASs were performed for early-phase expressive vocabulary, late-phase expressive vocabulary, and late-phase receptive vocabulary using METAL as part of stage I. To increase statistical power, multi-trait SNP-vocabulary associations were examined by combining genetically related vocabulary traits using MTAG as part of stage II. † Estimated sample size based on the increase in mean χ^2 statistic using MTAG. Abbreviations: CDI, Communicative Development Inventory; LDS, Language Development Survey; MA, meta-analysis; SNP, Single-Nucleotide Polymorphism

SNP-vocabulary associations



Single-trait (stage I) and multi-trait (stage II) SNP-vocabulary associations were assessed using METAL and MTAG, respectively. No SNP-vocabulary associations passed the adjusted threshold (red line, $P < 2.1 \times 10^{-6}$). rs9854781 was associated with early-phase expressive vocabulary at the unadjusted genome-wide significance threshold (blue line, $P < 5 \times 10^{-8}$). Genetic correlations among single-trait vocabulary summary statistics were derived with HDL. † Estimated sample size based on the increase in mean χ^2 statistic using MTAG. Abbreviations: HDL, High-Density Likelihood; MA, meta-analysis.

SNP-heritability of early vocabulary

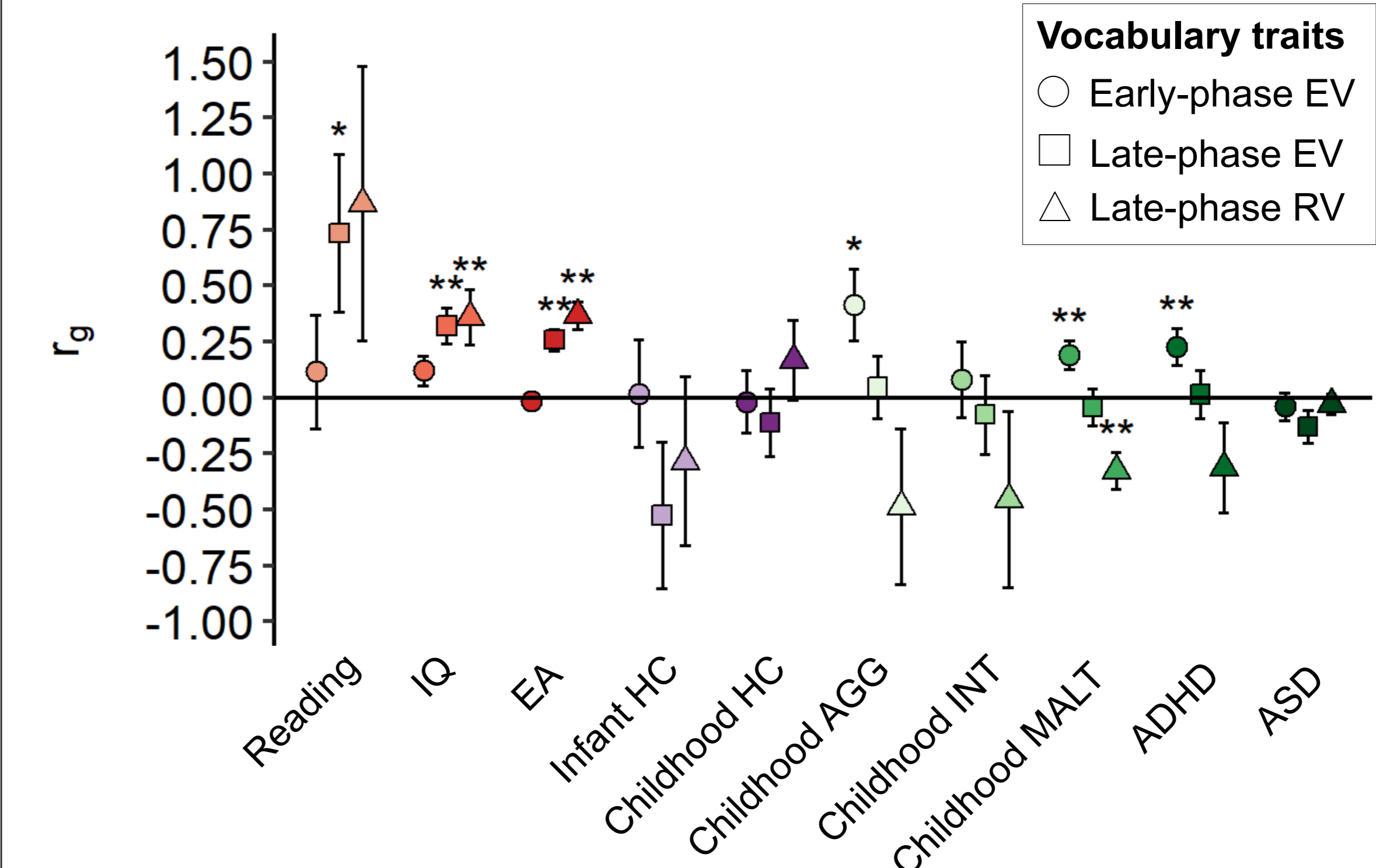
Analysis	Trait	SNP- h^2 (SE)	Z-score	P	N
Stage I: single-trait MA	Early-phase EV	0.24(0.02)	8.64	$< 1 \times 10^{-10}$	8,799
	Late-phase EV	0.08(0.01)	5.53	3×10^{-8}	19,296†
	Late-phase RV	0.20(0.04)	5.21	2×10^{-7}	6,291
Stage II: multi-trait MA	EV	0.10(0.01)	6.91	$< 1 \times 10^{-10}$	22,104†
	Late-phase vocabulary	0.07(0.01)	5.00	5×10^{-7}	23,466†

SNP-heritability (SNP- h^2), corresponding standard error (SE) and P-value were estimated with High-Density Likelihood (HDL) software using a HapMap3 reference panel. SNP- h^2 Z-scores were calculated by dividing SNP- h^2 by its standard error. † Estimated sample size based on the increase in mean χ^2 statistic using MTAG. Abbreviations: EV, expressive vocabulary; MA, meta-analysis

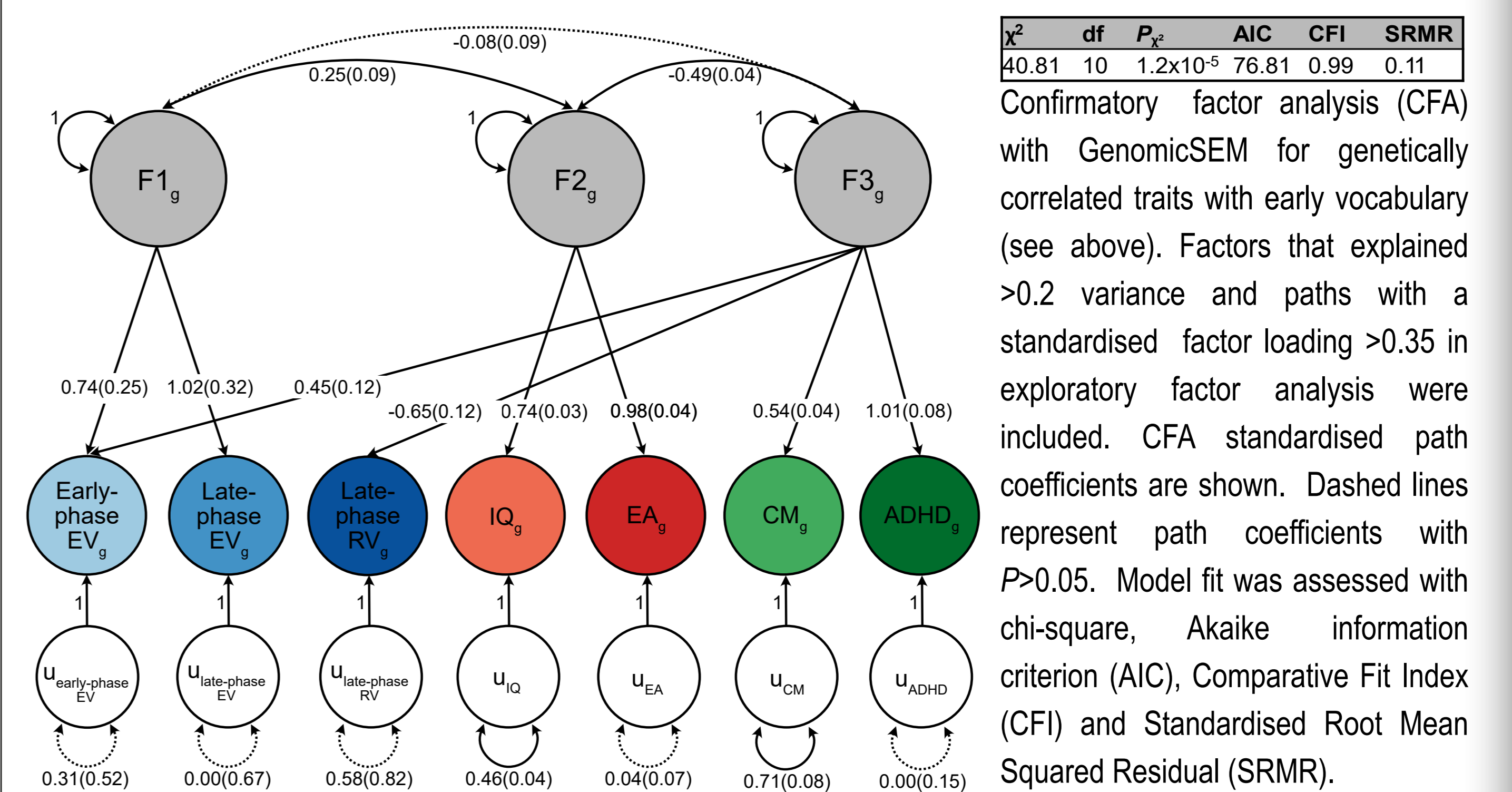
Gene-, gene-set and gene-property analyses

All analyses were carried out within FUMA software. No results passed multiple-testing-adjusted thresholds.

Genetic links with later-life cognitive, behavioral and health outcomes



Genetic correlations of vocabulary traits with later-life cognitive, behavioral and health outcomes estimated using HDL software. Bars represent standard errors. * $P < 0.05$; ** $P < 5.3 \times 10^{-3}$. Abbreviations: ADHD, Attention-Deficit/Hyperactivity Disorder; AGG, aggression; ASD, Autism Spectrum Disorder; EA, educational attainment; EV, expressive vocabulary; HC, head circumference; INT, internalising symptoms; IQ, general intelligence; MALT, maltreatment; RV, receptive vocabulary



In a nutshell - we found that ...

the genetic architecture underlying early vocabulary changes during development:

- genetic relationships with cognition trace back to word use and understanding in toddlerhood, but not infancy
- exposure to maltreatment in childhood has a negative genetic link with word understanding in toddlers, while the link with single-word production in infants is positive

