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TITLE: The Multivariate Genetic Architecture of Language- and Literacy-related Abilities.

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ABSTRACT:
Many measures of language, literacy and phonological working memory genetically overlap, though our knowledge of their hierarchical genetic architecture is limited. Here, we structurally modelled multivariate genetic variances between reading fluency, spelling, phonemic awareness, oral language and non-word repetition in up to 6,453 unrelated ALSPAC children with phenotypic and genome-wide information. Multivariate

genetic architectures where investigated with Genetic-relationship-matrix structural equation modelling (GSEM) using Cholesky and Independent Pathway models, and a combination of both models. The latter model structures the genetic variance as an Independent Pathway model (consisting of common and measurement-specific influences) and the residual variance according to a Cholesky decomposition. Model fit comparisons showed that the combined model fitted the data best. A single shared genetic factor explained the majority of genetic variance in non-word, word and passage reading fluency, ranging between 93%(SE=4%) for passage reading accuracy (9 years) and 82% (SE=9%) for word reading speed (13 years). Utilizing passage reading accuracy as a proxy of reading fluency, we identified a shared genetic factor that explained genetic variance in reading (97%(SE=0.08)), spelling (91%(SE=0.08)), phonemic awareness (98%(SE=0.10)), oral language (44%(SE=0.14)) and non-word repetition (53% (SE=0.14)). Factor structures were robust for different proxy measure selections. Measurement-specific genetic factor contributions to SNP-h^2 were found for oral language(56%(SE=0.14)) and non-word repetition (47%(SE=0.14)) and also for other reading fluency proxies, such as word reading speed at 13 years (44%(SE=0.14)). Hence, multiple cognitive skills contribute to literacy and language performance involving pleiotropic influences augmented by measurement-specific genetic factors.

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