

CONTRIBUTION OF POLYGENIC SCORES FOR A “COMMON EXECUTIVE FUNCTION” FACTOR TO COGNITIVE PERFORMANCE IN THE PSYCOURSE STUDY

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BACKGROUND

Executive Functions (EFs) are meta-cognitive functions that control and coordinate mental processes (e.g., Friedman and Robbins, 2022). Importantly, impaired EFs are a hallmark of many psychiatric disorders. On the phenotype level, EFs include processes such as inhibition, set-shifting, and working memory, and there is substantial evidence that these higher-level cognitive functions are (1) best assessed on a latent level, (2) related to but distinct from general intelligence, (3) highly heritable, (4) highly polygenic, and (5) associated with the prefrontal cortex (Friedman and Miyake, 2017). Recently, a large-scale UK Biobank GWAS has examined the genomics of this Common EF factor and found it to be associated with fast synaptic processes, and genetically correlated to psychiatric disorders (Hatoum et al., 2022). Here, we assess the contribution of polygenic scores (PS) for the Common EF factor to cognitive test performance measured in the transdiagnostic PsyCourse Study (Budde et al., 2019).

METHODS

We used PRS-CS (Ge et al., 2019) to calculate PS from summary statistics of the Common EF factor GWAS (Hatoum et al., 2022) in a subsample (N=1594) of The PsyCourse Study (n=404 neurotypic, n=574 psychotic, n=616 affective), which were genotyped on the Illumina Infinium Global Screening Array and assessed according to DSM-IV or ICD-10 criteria. The following standardized cognitive tests were assessed: Trail-Making-Test (TMT, parts A and B), Verbal Digit Span (forward and backward), Digit Symbol Test, a Vocabulary Intelligence Test, and a Verbal Learning Test. For each cognitive test, we used a baseline model comprising the following independent variables: age, age², sex, diagnosis, and the first four components of an ancestry principal components analysis. The residuals of this model were then regressed onto PS of the Common EF factor. Where appropriate, data transformation or dichotomization of test scores was applied.

Common Executive Function Polygenic Scores in The PsyCourse Study

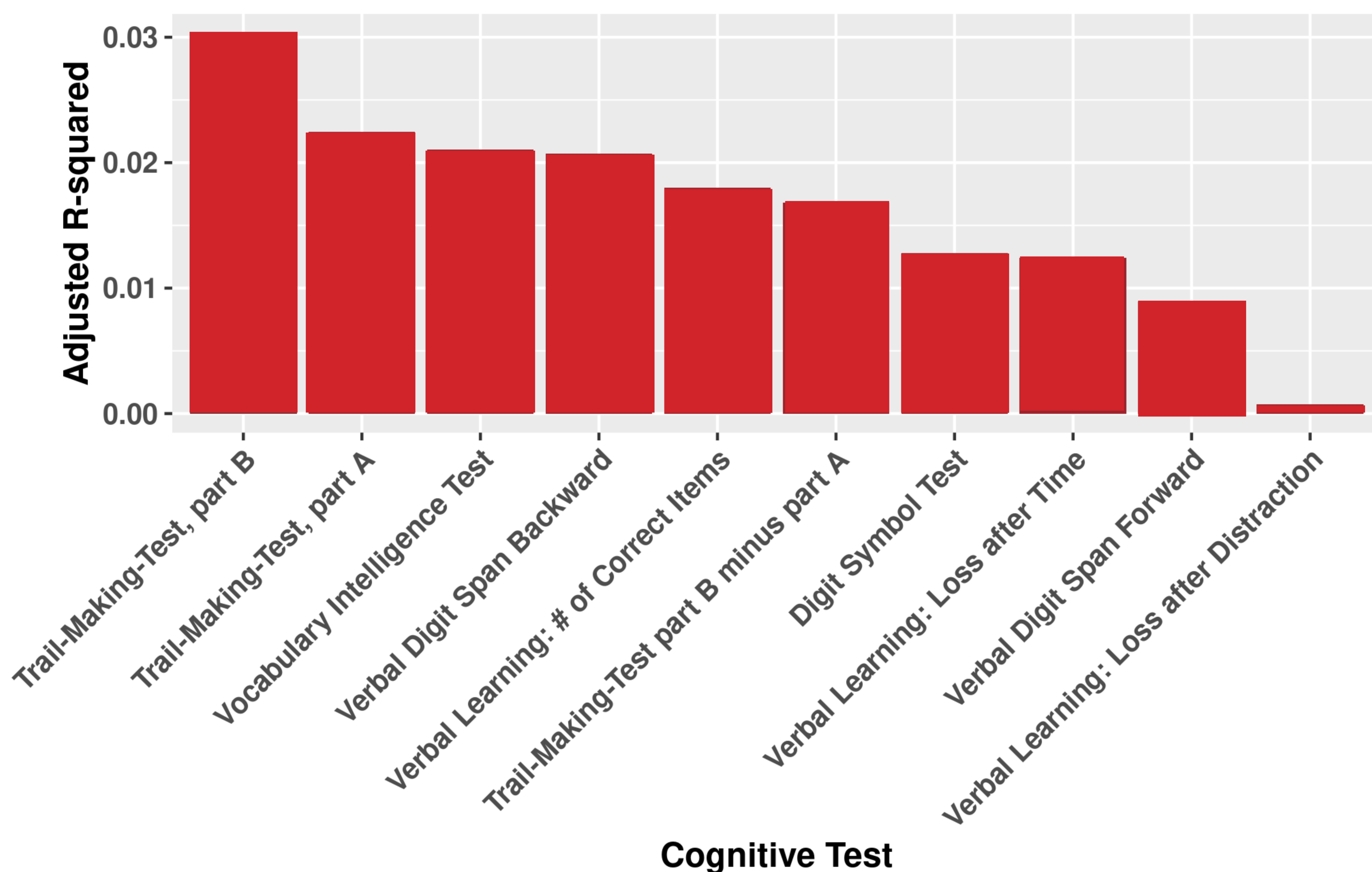


Figure 1. Proportion of explained variance in cognitive test performance by PS for the Common EF factor.

RESULTS

We observed that PS for the Common EF factor explained a significant part of cognitive test performance (Figure 1), with one exception (Verbal Learning: Loss after Distraction).

DISCUSSION

Common EF PS capture a small but significant proportion of the variance of most cognitive tests assessed in The PsyCourse Study. As expected, Common EF PS show the largest effect size in a classical EF tests, namely Part B of the Trail-Making-Test. Our analysis confirms the utility of Common EF PS in future cognitive and psychiatric studies.

REFERENCES

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