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Computational Modeling of the n-Back Task in the ABCD Study: Associations of Drift Diffusion Model Parameters to Polygenic Scores of Mental Disorders and Cardiometabolic Diseases

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ABSTRACT

BACKGROUND: Cognitive dysfunction is common in mental disorders and represents a potential risk factor in childhood. The nature and extent of associations between childhood cognitive function and polygenic risk for mental disorders is unclear. We applied computational modeling to gain insight into mechanistic processes underlying decision making and working memory in childhood and their associations with polygenic risk scores (PRSs) for mental disorders and comorbid cardiometabolic diseases.

METHODS: We used the drift diffusion model to infer latent computational processes underlying decision making and working memory during the n-back task in 3707 children ages 9 to 10 years from the Adolescent Brain Cognitive Development (ABCD) Study. Single nucleotide polymorphism–based heritability was estimated for cognitive phenotypes, including computational parameters, aggregated n-back task performance, and neurocognitive assessments. PRSs were calculated for Alzheimer's disease, bipolar disorder, coronary artery disease (CAD), major depressive disorder, obsessive-compulsive disorder, schizophrenia, and type 2 diabetes.

RESULTS: Heritability estimates of cognitive phenotypes ranged from 12% to 38%. Bayesian mixed models revealed that slower accumulation of evidence was associated with higher PRSs for CAD and schizophrenia. Longer nondecision time was associated with higher PRSs for Alzheimer's disease and lower PRSs for CAD. Narrower decision threshold was associated with higher PRSs for CAD. Load-dependent effects on nondecision time and decision threshold were associated with PRSs for Alzheimer's disease and CAD, respectively. Aggregated neurocognitive test scores were not associated with PRSs for any of the mental or cardiometabolic phenotypes.

CONCLUSIONS: We identified distinct associations between computational cognitive processes and genetic risk for mental illness and cardiometabolic disease, which could represent childhood cognitive risk factors.

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Mental disorders are highly complex, heritable, and polygenic (1). Aggregating many small effects of common single nucleotide polymorphisms (SNPs) on mental disorders from genome-wide association studies (GWASs) allow for the construction of polygenic risk scores (PRSs), reflecting an individual's cumulative genetic risk for a given trait or disorder. Mapping PRSs for adult-onset disorders to relevant phenotypes in childhood represents an opportunity for discovering the expression of genetic liability in premorbid phases.

Cognitive functions are also heritable traits (2–4), and cognitive deficits are frequent in patients with mental disorder (5,6). Working memory (WM) dysfunction is commonly reported in mental disorders including schizophrenia (SZ) (7), bipolar disorder (8), and major depressive disorder (MDD) (9), while impaired decision making is observed in, among others, obsessive-compulsive disorder (10), MDD (11), and SZ (12,13).

Deficits in cognition have been found to precede the onset of illness, in some cases during childhood (14–17). Whether cognitive aberrations during childhood are associated with genetic liability for mental disorders is currently being explored. Recent studies have found PRSs for SZ to be positively associated (18), negatively associated (19), and not associated (20,21) with general cognitive function in childhood and adolescence, while others have reported negative associations between PRSs for Alzheimer's disease (AD) and memory (22) and between PRSs for SZ and emotion identification and verbal reasoning (23). It is currently unclear how cognitive variability in childhood is reflected in genetic liability for other mental disorders. Further, it is unclear how cognitive function

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relates to polygenic risk for cardiometabolic disease, which, partly owing to shared genetic risk (24), is highly comorbid with mental disorders (25,26) and, together with mental illness, is one of the largest causes of disability, morbidity, and mortality worldwide (27,28). Further, cardiometabolic diseases have previously been linked to cognitive aberration (29–31). Taken together, an improved understanding of cognitive deficits during childhood for mental and cardiometabolic diseases with adult onset could give insight into the mapping between cognition and mental and cardiometabolic disease risk.

Cognitive abilities are often inferred from observed behavior such as task accuracy or response time. Although identifying associations between mental disorders and observed behavior can have predictive value, measures of task accuracy and response time are inherently agnostic about their computational origins. For example, poor accuracy could result from impulsive decision making or from a low signal-to-noise ratio in information accumulation. Computational approaches, in contrast, allow for model-based delineations of latent cognitive processes (32) and have provided insight into the computational cognitive processes underlying aberrant learning and decision making in clinical groups (33–36). Further, individual-level parameters from computational models have been shown to be more sensitive to diagnosis (37) and clinical outcome (38) than task accuracy and response time.

Thus, computational modeling could aid in identifying mechanistic cognitive processes associated with genetic liability for mental disorders. To this end, we took a computational psychiatry (39) approach to map associations between latent cognitive processes and PRSs for mental disorders. We applied the drift diffusion model (DDM) (40) to performance on the n-back task, a decision-making task probing WM capacity, from 3707 children ages 9 to 10 years in the Adolescent Brain Cognitive Development (ABCD) Study (41–44) baseline sample. DDM analysis allowed us to estimate individual computational parameters during 2 load conditions (0-back and 2-back), including evidence accumulation, speed-accuracy tradeoff, response bias, and time spent on motor and perceptual processes. PRSs were calculated for AD (45), bipolar disorder (46), MDD (47), obsessive-compulsive disorder (48), and SZ (49). In addition, we calculated PRSs for coronary artery disease (CAD) (50) and type 2 diabetes (51).

We used genome-wide complex trait analysis (52) to assess whether DDM parameters represent heritable traits. Next, we tested for associations between DDM parameters and PRSs using Bayesian linear multilevel models, which allowed us to describe uncertainty in estimates. To provide a comparison to DDM parameters, we also tested for associations with response time and task accuracy, as well as aggregated neuropsychological scores as a proxy for general cognitive ability.

METHODS AND MATERIALS

Participants

The total sample consists of 11,875 children ages 9 to 10 years. We analyzed data made available through the curated data release 2.0.1 (DOI:10.15154/1504041). Informed written consent for children and parents was obtained from parents, and child participants separately completed a written assent.

n-Back Task

The emotional n-back task (53,54) consisted of 160 trials divided into 2 runs. The task was performed in the scanner while collecting functional magnetic resonance imaging data. Each run consisted of 8 blocks, each with 10 trials. For each trial, the objective was to decide whether the current stimulus matched a target stimulus (Figure 1A). In the 0-back condition, the target stimulus was presented before the first trial in each block, and the participants were asked to decide whether the current stimulus matched the target stimulus. In the 2-back condition, participants responded whether the stimulus on the current trial matched the stimulus presented 2 trials back. The stimulus and target matched in 20% of the trials. For the remaining trials, the stimulus did not match the target, and the stimulus on the current trial either had (lure, 25% of trials) or had not (nonlure, 55%) been presented earlier in the block.

Stimulus category (house and happy, fearful, or neutral faces) varied across blocks but was not incorporated into these analyses, because it would result in too many parameters for reliable subject-level estimates. Information regarding the condition (and, for the 0-back condition, the target stimulus) was presented for 2500 ms at the start of each block. The stimulus was preceded by a plus sign presented for 1000 ms. The stimulus and the stimulus-response mapping were presented for 2000 ms.

The analysis included data from participants with recorded response on at least 50 of the total 160 trials to ensure reliable measures of performance. A total of 8077 participants fulfilled this criterion. Data on one or more variables of interest were missing from 248 participants (Table S1), for which data were imputed using the R package “mice” (55). Participants with a task accuracy below 60% (n = 468) were excluded, resulting in a sample of 7609 participants, which were included in the heritability analysis. Next, because the PRSs were derived from samples of European ancestry, we excluded participants of non-European origin, which included 3707 participants.

Drift Diffusion Model

We analyzed trial-by-trial choice and response time data on the n-back task with the DDM, a cognitive process model that describes two-alternative forced choice decision making as a noisy accumulation-to-bound process (Figure 1B). The DDM provides good fits to observed choice and response time distributions (56). The accumulation-to-bound processes proposed by sequential sampling models, including the DDM, have been shown to correlate with neural firing patterns during decision making in primates, suggesting that the model captures neural implementations of decision making, providing a link between behavior and neural activity (57).

The DDM has 4 main parameters. Drift rate (v) reflects the rate of evidence accumulation, where stronger drift rate leads to faster and more accurate decisions, due to less impact of noise. Decision threshold (a) captures the speed-accuracy tradeoff, where wider decision thresholds require more evidence to be accumulated to reach a decision. This will lead to slower, but more accurate, decisions. The starting point bias parameter (z) captures the starting point of the accumulation process. Finally, nondecision time (ndt) captures the time spent on encoding the stimulus and motor response, where

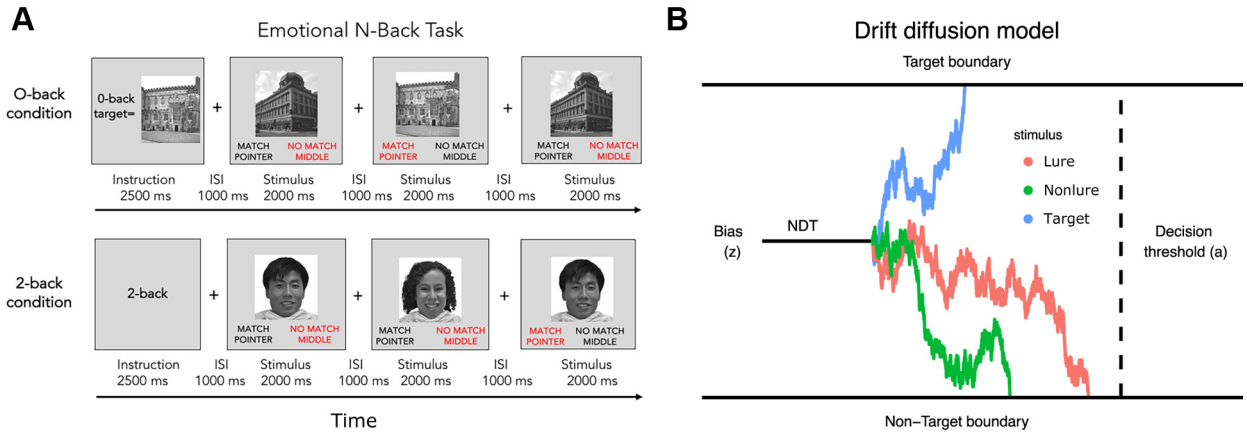

Figure 1. **(A)** Emotional n-back task. During the 0-back condition (top), participants were instructed to decide whether a stimulus matched the target stimulus presented at the start of each block. During the 2-back condition (bottom), participants were instructed to decide whether the currently presented stimulus matched the stimulus presented 2 trials back. **(B)** Illustration of the drift diffusion model applied to the n-back task. The model assumes that decision makers accumulate evidence until reaching a threshold to decide whether the current stimulus is a target (upper bound) or nontarget (lower bound). Illustrated here are 3 simulated decisions, one for each stimulus type (lure, nonlure, and target). The rate and direction at which evidence is accumulated depends on the drift rate. Here, sample paths were simulated with a drift rate of −2.5 (lure), −2.3 (nonlure), and +3.05 (target). ISI, interstimulus interval; NDT, nondecision time. Figure adapted with permission from (42).

shorter nondecision time reflects that less time is spent on stimulus encoding and motor response. The parameters of the DDM can be estimated using the Wiener first passage time likelihood function (58) and thus allows inference on how parameters vary between groups, individuals, and task manipulations.

n-Back DDM. For the n-back task, we assumed that participants could be biased toward responding target or nontarget, and therefore we coded upper bound responses as target responses and lower bound responses as nontarget (Figure 1B). We allowed the rate of evidence accumulation to differ across stimulus type and thus estimated separate drift rates for target, lure, and nonlure stimuli. Further, to capture effects of load, we estimated all parameters separately for the 0-back and 2-back conditions. In total, 12 parameters were estimated per subject in a mixed model using the Wiener first passage time distribution to calculate the likelihood of the response times of choices (x),

$$RT(x) \sim Wiener(a_{s,c}, ndt_{s,c}, z_{s,c}, v_{s,c,stim}),$$

where a = decision threshold, c = condition (0-back or 2-back), ndt = nondecision time, RT = response time, s = subject, $stim$ = stimulus (target, lure, nonlure), v = drift rate, x = choice (target or nontarget), and z = starting point bias. In addition, we estimated group-level variability parameters for nondecision time.

To reduce the number of variables, we computed overall scores for each of the 4 cognitive processes from the 12 estimated parameters, i.e., an average individual value for decision threshold, nondecision time, drift rate, and starting point bias across conditions and stimuli. We further calculated load effects for each parameter by subtracting estimates for the 0-back from the 2-back condition.

Figure 2A and B shows that the model fit was good and that predicted choice, response time, and response time distributions (Figure S1) across conditions closely matched the observed data. Briefly, Figure 2C shows that reduced accuracy and slower response times in the 2-back condition compared with the 0-back condition were reflected as lower drift rate in the 2-back condition, with the strongest effect for lures, likely reflecting a higher propensity to mistake lures for targets. Participants were more biased toward responding target in the 2-back condition, reflected in an increased starting point bias toward the target boundary. Finally, participants increased the decision threshold in the 2-back condition compared with the 0-back condition, which counteracts the effect of higher difficulty on accuracy but also leads to slower responses.

NIH Toolbox

Participants completed the NIH Toolbox (http://www.nihtoolbox.org), a computerized test battery composed of 7 tasks spanning executive function, WM, episodic memory, attention, processing speed, and language (59). We performed principal component analysis on uncorrected scores from all 7 tasks and included the first component in analyses as a measure of general cognitive ability. See (60) for more details.

Figures S2 and S3 show the distribution and scatter plots of the included variables across participants.

Statistical Analysis

Drift Diffusion Model. We used the python package HDDM (61) to model choice and response time data from the n-back task with Bayesian hierarchical estimation. Because running all subjects in a single model would be too time consuming, we randomly assigned subjects to one of 40 groups and ran Bayesian hierarchical models for each of these 40 groups.

Three chains, each with 2000 samples, were estimated for each group. The first 1000 samples were discarded as burn-in to allow the sampling process to identify the region of best-fitting values in the parameter space. The models were

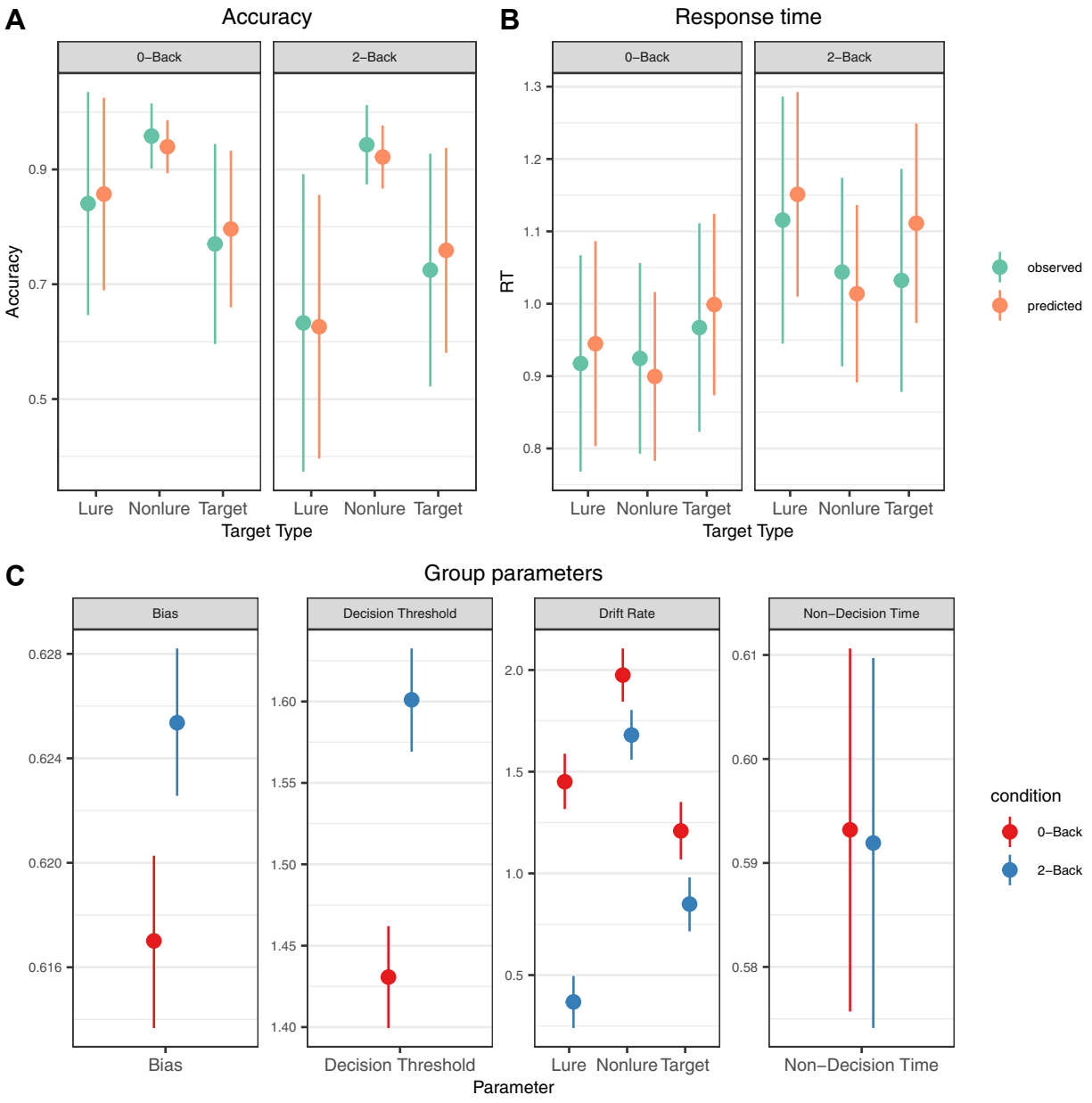

Figure 2. Model fit and group parameter estimates. **(A, B)** Observed (green) and predicted (orange) mean and standard deviation accuracy **(A)** and response time (RT) **(B)** across condition (0-back and 2-back) and stimuli (lure, nonlure, target). The model slightly overpredicted accuracy for target responses, while accuracy for nonlures was slightly underpredicted. The model shows a good prediction of the RT distribution but slightly overpredicts mean RT for targets in the 2-back condition. **(C)** Mean estimated parameters and their 95% highest-density interval across 0-back (red) and 2-back (blue) conditions and, for drift rate, stimuli (lure, nonlure, target). Positive (negative) drift rate values indicate that evidence is accumulated toward responding target (nontarget).

estimated to be reliable, meaning that rerunning the models yielded similar parameter estimates. This was measured with the Gelman-Rubin statistic (62), which was below 1.1 for all group and subject parameters, indicating convergence. Scripts for HDDM analyses can be found at https://osf.io/ubezy/.

Genetic Data. Genotyping on saliva samples collected at the baseline visit was performed using the Smokescreen array, consisting of 646,247 genetic variants. Following (63), we removed genetic variants that were not called in at least 95% of the sample and individuals with more than 20% missing data. Variant imputation was performed on 517,724 SNPs and 10,659 participants with the Michigan Imputation Server using the hrc.r1.1.2016 reference panel, Eagle v.2.3 phasing, and multiethnic imputation process. PLINK (64) was used to convert dosage files to plink files, using a best guess threshold

of 0.9 for each locus. Further, PLINK was used for post-imputation quality control, filtering out variants with an imputation INFO score below 0.5, a minor allele frequency below 0.001, failing Hardy-Weinberg equilibrium at $p = 1 \times 10^{-9}$, and missingness above 5%, as well as individuals missing more than 10% of variants. After these steps, 14,754,215 SNPs and 10,660 individuals remained.

Heritability. We used the GCTA-GREML analysis (54,65,66) in genome-wide complex trait analysis (52) to simultaneously estimate SNP-based and pedigree-based heritability of DDM parameters, response time, accuracy, and NIH Toolbox scores using a relatedness threshold of 0.05 and 20 ancestry components of the genetic relationship matrix as covariates. Here, we report SNP-based heritability.

Polygenic Risk Scores. Using PRSice v.2 (67), we calculated PRSs for AD (45), bipolar disorder (46), CAD (50), MDD (47), obsessive-compulsive disorder (48), SZ (49), and type 2 diabetes (51). We processed the GWAS summary statistics using a standardized pipeline (https://github.com/precimed/python_convert) and ran PRSice using default settings. We performed principal component analysis on PRSs across all p thresholds and used the first component of this analysis to associate to cognitive phenotypes.

Bayesian Linear Multilevel Models. We tested for associations between cognitive phenotypes (computational parameters, mean response time and accuracy from the n-back task, WM load effects for computational parameters, response time and accuracy, and the first principal component calculated from the NIH Toolbox) and PRSs with Bayesian linear multilevel models using brms (68) built on top of Stan (69). Models were run for all combinations of cognitive phenotypes and PRSs. Further, we tested the effect of load by computing the difference between parameter estimates (and response time and accuracy) between the 2-back and 0-back conditions. All models included sex and age as fixed effects and scanning site, family (siblings and twins), and model group (40 pools of subjects used for DDM analysis) as random effects:

$$\textit{cognitive phenotype} \sim \textit{PRS} + \textit{age} + \textit{sex} + (1|\textit{site}) + (1|\textit{family}) + (1|\textit{model group})$$

Models also included 10 genetic ancestry principal components and genetic batch as covariates. Priors strongly centered around 0 (mean = 0, SD = 0.5) were used for all coefficients to reduce the likelihood of false positives. All variables were standardized prior to analysis. To assess whether measures of socioeconomic status influenced the association of cognitive phenotypes and polygenic risk, we ran additional models including family income, marital status, and highest education of caregivers as covariates. Scripts for Bayesian linear multilevel model analyses can be found at https://osf.io/ubezy/.

Statistical Inference. We describe the effect size of predictors as the mean and 95% highest-density interval of posterior distributions (70).

RESULTS

SNP-Based Heritability

Individual differences in DDM parameters showed moderate SNP heritability (decision threshold: h^2 = 0.15, SE = 0.05; nondecision time: h^2 = 0.19, SE = 0.05; drift rate: h^2 = 0.23, SE = 0.05; bias: h^2 = 0.12, SE = 0.06). Similar results were found for response time (h^2 = 0.16, SE = 0.05) and accuracy (h^2 = 0.21, SE = 0.05), while heritability of the first principal component from the NIH Toolbox was estimated to be h^2 = 0.38 (SE = 0.05).

Associations Between Cognitive Phenotypes and PRSs

Figure 3 and Table 1 summarize results from the Bayesian linear multilevel models estimating the association between cognitive phenotypes and PRSs for mental illness and cardiometabolic disease. Figure S4 shows the strong overlap between posterior distributions for models that included family income, marital status, and highest education of caregivers as covariates. Further, Figure S5 shows the estimated interaction of all combinations of polygenic risk for mental illness and cardiometabolic disease on cognitive phenotypes. Finally, Figure S6 shows the association of cognitive phenotypes from the n-back task for each condition and contrasted for stimulus type.

Higher PRSs for AD were associated with slower responses (beta = 0.05, 95% highest-density interval = [0.01 to 0.08]), reflected in longer nondecision time (0.04 [0.01 to 0.07]).

Higher PRSs for CAD were associated with lower accuracy (−0.04 [−0.08 to −0.01]) and faster responses (−0.05 [−0.08 to −0.01]), reflected in lower drift rates (−0.05 [−0.08 to −0.01]) and faster nondecision times (−0.07 [−0.1 to −0.03]).

Higher PRSs for SZ were also associated with lower task accuracy (−0.04 [−0.07 to −0.01]), reflected in lower drift rates (−0.04 [−0.08 to −0.01]).

WM contrasts, captured as the difference between 2-back and 0-back conditions in the n-back task, were found to be negatively associated with PRSs for AD (−0.04 [−0.07 to −0.003]) on nondecision time and with PRSs for CAD on decision thresholds (−0.04 [−0.08 to −0.003]).

None of the polygenic scores were associated with the first principal component from the NIH Toolbox (Table 1).

DISCUSSION

Cognitive impairments are frequently observed in patients with mental disorders and often precede the emergence of clinical symptoms (71). While not included among the diagnostic criteria, mapping specific cognitive functions to PRSs for mental illness in children could provide new knowledge on the cognitive architecture of psychopathology.

We used computational modeling to identify and associate latent variables of decision making and WM in 3707 children to PRSs for mental illness and cardiometabolic disease. Individual variation in computational parameters were reflected in genetic variability, suggesting that the parameters represent heritable phenotypes. We found small but robust associations between DDM parameters and PRSs for mental illness and

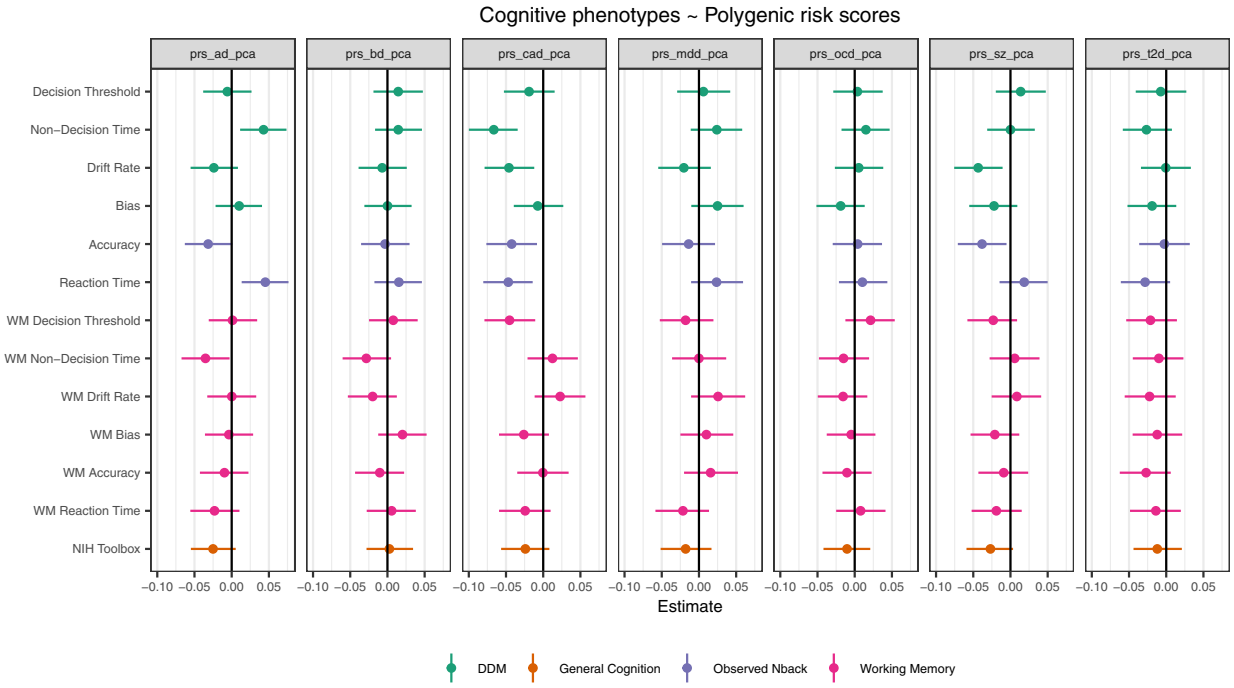

Figure 3. Posterior distributions for the association of polygenic scores on cognitive phenotypes. Error bars represent 95% highest-density interval. ad, Alzheimer's disease; bd, bipolar disorder; cad, coronary artery disease; DDM, drift diffusion model; mdd, major depressive disorder; NIH Toolbox, first principal component from the NIH cognitive test battery; ocd, obsessive-compulsive disorder; pca, principal component analysis; prs, polygenic risk score; sz, schizophrenia; t2d, type 2 diabetes; WM, working memory.

cardiometabolic disease. The cognitive measures associated with PRSs were related to task performance across load conditions, and to a lesser extent to effects of load, suggesting a link to decision making in general and not to aberrations in WM.

We did not find any associations of genetic liability to general cognitive function, as reflected in the first principal component of the neurocognitive battery. If this reflects a true null effect, it suggests that general cognitive dysfunction in, e.g., SZ is linked to nongenetic factors (72), has a later onset than the specific processes captured by the n-back task, and/or reflects that PRSs, as approximations of the underlying genetic variability associated with mental illness, do not capture these associations fully. Alternatively, the decomposition of general cognitive function may have favored some common or latent cognitive processes not associated with genetic liability of mental illness. Finally, it is possible that nonrandom study sampling processes influence the associations and subsequent interpretations. Previous findings from a similar U.S.-based youth sample have indicated a positive association between PRSs for SZ and IQ (18), which may arise if individuals with both high genetic risk and low function are not represented in the sample for various reasons. Future ABCD studies including information on familial risk and prevalence and later development of mental illness in the participants may be able to delineate some of these potential confounders.

Our analyses revealed several associations between DDM parameters and PRSs. We also identified comparable associations and heritability estimates of response time and accuracy. However, computational modeling is assumed to give insight into the latent computational processes that give rise to alterations in observed behavior and, as such, represent phenotypes potentially more closely related to brain function.

Higher PRSs for AD were associated with slower responses, which were captured by the DDM as longer nondecision time. Slowed reaction time has been suggested as an early sign of AD and has been identified as being partly driven by longer nondecision times, which encompass time spent on sensory encoding and motor output (73). Premorbid cognitive dysfunction has been shown in preclinical AD and as a predictor of progression from mild cognitive impairment to AD in older adults (16,74). Associations between PRSs for AD and nondeclarative memory, but not executive memory, in children ages 6 to 14 years has been reported (22). Longitudinal studies could test whether these cognitive profiles are predictive of AD over and above PRSs.

Higher PRSs for SZ were associated with slower evidence accumulation and lower accuracy. These results are in line with case-control studies reporting impairment in SZ for decision making (12,13). Previous studies have reported negative (19,75), positive (18), and no associations (21,76,77) between PRSs for SZ and cognitive function across age spans in the general population. A longitudinal study showed that polygenic risk for SZ was not associated with childhood cognitive performance, but rather with the rate of cognitive decline from ages 11 to 70 years (78). These results were based on general

Table 1. Posterior Distributions of Associations Between Cognitive Phenotypes and Clinical and Polygenic Scores

Cognitive Phenotype	PRS AD	PRS BD	PRS CAD	PRS MDD	PRS OCD	PRS SZ	PRS T2D
Decision Threshold	−0.006 (−0.038 to 0.027)	0.014 (−0.019 to 0.048)	−0.019 (−0.053 to 0.015)	0.006 (−0.029 to 0.042)	0.004 (−0.029 to 0.038)	0.014 (−0.02 to 0.047)	−0.07 (−0.041 to 0.027)
Drift Rate	−0.024 (−0.055 to 0.008)	−0.007 (−0.039 to 0.026)	−0.046 (−0.079 to −0.012)	−0.02 (−0.055 to 0.016)	0.005 (−0.027 to 0.038)	−0.043 (−0.076 to −0.011)	−0.001 (−0.034 to 0.033)
Nondecision Time	0.042 (0.011 to 0.074)	0.015 (−0.017 to 0.046)	−0.066 (−0.1 to −0.034)	0.024 (−0.011 to 0.058)	0.015 (−0.018 to 0.047)	−0.00 (−0.031 to 0.033)	−0.027 (−0.058 to 0.004)
Bias	0.01 (−0.022 to 0.041)	0.00 (−0.031 to 0.032)	−0.007 (−0.04 to 0.027)	0.025 (−0.01 to 0.06)	−0.019 (−0.051 to 0.013)	−0.022 (−0.055 to 0.009)	−0.019 (−0.052 to 0.013)
WM Accuracy	−0.01 (−0.043 to 0.023)	−0.01 (−0.044 to 0.022)	−0.00 (−0.035 to 0.034)	0.011 (−0.026 to 0.046)	−0.01 (−0.043 to 0.024)	−0.009 (−0.043 to 0.024)	−0.027 (−0.062 to 0.006)
WM Reaction Time	−0.023 (−0.056 to 0.01)	0.006 (−0.028 to 0.038)	−0.024 (−0.059 to 0.01)	−0.022 (−0.059 to 0.014)	0.007 (−0.026 to 0.041)	−0.019 (−0.052 to 0.015)	−0.014 (−0.049 to 0.02)
WM Drift Rate	0 (−0.032 to 0.033)	−0.02 (−0.053 to 0.013)	0.023 (−0.012 to 0.057)	0.026 (−0.011 to 0.062)	−0.016 (−0.5 to 0.017)	0.009 (−0.025 to 0.041)	−0.021 (−0.056 to 0.013)
WM Decision Threshold	0.002 (−0.033 to 0.033)	0.008 (−0.025 to 0.041)	−0.045 (−0.079 to −0.011)	−0.018 (−0.053 to 0.019)	0.021 (−0.013 to 0.054)	−0.023 (−0.058 to 0.009)	−0.021 (−0.054 to 0.014)
WM Nondecision Time	−0.035 (−0.07 to −0.003)	−0.028 (−0.06 to 0.005)	0.012 (−0.021 to 0.047)	−0.00 (−0.036 to 0.037)	−0.015 (−0.048 to 0.019)	0.006 (−0.028 to 0.039)	−0.01 (−0.041 to 0.023)
WM Bias	−0.004 (−0.036 to 0.03)	0.02 (−0.012 to 0.053)	−0.026 (−0.059 to 0.008)	0.001 (−0.025 to 0.046)	−0.005 (−0.038 to 0.028)	−0.021 (−0.054 to 0.012)	−0.012 (−0.045 to 0.023)
Response Time	0.045 (0.013 to 0.076)	0.015 (−0.017 to 0.046)	−0.047 (−0.081 to −0.014)	0.022 (−0.013 to 0.056)	0.012 (−0.02 to 0.044)	0.018 (0.015 to 0.05)	−0.028 (−0.061 to 0.005)
Accuracy	−0.032 (−0.063 to 0.001)	−0.003 (−0.035 to 0.03)	−0.042 (−0.076 to −0.006)	−0.013 (−0.048 to 0.023)	0.005 (−0.029 to 0.037)	−0.038 (−0.071 to −0.005)	−0.003 (−0.036 to 0.032)
NIH Toolbox	−0.025 (−0.055 to 0.005)	0.008 (−0.028 to 0.034)	−0.024 (−0.057 to 0.008)	−0.018 (−0.052 to 0.015)	−0.003 (−0.034 to 0.028)	−0.027 (−0.059 to 0.003)	−0.021 (−0.044 to 0.021)

Values are given in mean (95% HDI).

AD, Alzheimer's disease; BD, bipolar disorder; CAD, coronary artery disease; HDI, highest-density interval; MDD, major depressive disorder; NIH Toolbox, first principal component from the NIH cognitive test battery; OCD, obsessive-compulsive disorder; PRS, polygenic risk score; SZ, schizophrenia; T2D, type 2 diabetes; WM, working memory.

cognitive function, for which we did not find an association. Instead, focusing on domain-specific cognitive functions and their computational processes could be more sensitive to underlying aberrations captured by genetic liability.

Given the strong association between mental illness and cardiometabolic disease, we also tested for interactions of all combinations of PRSs for psychiatric disorders and cardiometabolic health (Figure S5). Despite revealing 5 weak associations, none of these were found to amplify main effects, i.e., they did not indicate that a high risk for both mental and cardiometabolic risk is even more strongly associated with cognition.

Although WM is strongly linked to mental disorder through case-control studies (7–9), our analyses did not identify associations between reduced WM capacity (captured as reduced accuracy or drift rate) and heightened polygenic risks for the included mental and cardiometabolic disorders. The only polygenic associations to WM load were altered adjustment of speed-accuracy tradeoff for CAD and changes in nondecision time for AD, which was not reflected in task accuracy or response time.

Although the first principal component from the NIH Toolbox was estimated to be more than twice as heritable as phenotypes from the n-back task, we found no associations to PRSs. These results are in line with previous studies reporting no associations between polygenic risk for mental illness and general cognitive function (21,76,77). Future investigations of follow-up data from the ABCD Study can indicate whether speeded decision making and not WM capacity or general cognitive ability are predictive of mental illness in adolescence.

The work described here is not without limitations. First, the computational parameters from the DDM cannot identify the separate contributions of WM components, including active maintenance and updating of target stimuli and inhibition of non-N stimuli. Although biophysical models of these processes exist (79), to our knowledge, they cannot be used for model fitting on a subject level [see (80) for computational modeling of an alternative WM task]. Second, because of the block design used for functional magnetic resonance imaging scans, which does not allow insight into trial-by-trial brain activity, we did not analyze the accompanying functional magnetic resonance imaging data and therefore cannot describe the association between computational parameters and their neural underpinnings. Third, because the GWAS summary statistics used to compute PRSs were based on individuals of European ancestry, we chose to limit our multilevel models with PRSs to participants of European descent. This limits the generalizability of our findings. Future GWASs should include a broader spectrum of populations in their sample.

In conclusion, we identified associations between computational cognitive processes and PRSs for mental illness and cardiometabolic disease in children ages 9 to 10 years. Recent studies have shown that the associations between psychological variables and mental disorders in large datasets typically are small (81), likely reflecting the decreased likelihood of false positives (and false negatives) (82). The results reported here are no different, suggesting that cognition generally, and decision making and WM specifically, is only one of many factors associated with the development of severe mental illness. However, mapping the associations between computational cognitive processes and genetic load for mental disorders can improve our understanding of the small but robust effects that do exist and assist in parsing the massive heterogeneity of mental disorders (83,84). Future studies could use follow-up data from the ABCD Study to identify how WM and decision-making capacity predict problem behavior, mental disorders, and cardiometabolic health later in adolescence.

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This article reflects the views of the authors and may not reflect the opinions or views of the NIH or ABCD consortium investigators.

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