


## ORIGINAL ARTICLE

# The relationship between temperament, polygenic score for intelligence and cognition: A population-based study of middle-aged adults

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## Abstract

We investigated whether temperament modifies an association between polygenic intelligence potential and cognitive test performance in midlife. The participants ( $n = 1647$ , born between 1962 and 1977) were derived from the Young Finns Study. Temperament was assessed with Temperament and Character Inventory over a 15-year follow-up (1997, 2001, 2007, 2012). Polygenic intelligence potential was

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assessed with a polygenic score for intelligence. Cognitive performance (visual memory, reaction time, sustained attention, spatial working memory) was assessed with CANTAB in midlife. The PGSI was significantly associated with the overall cognitive performance and performance in visual memory, sustained attention and working memory tests but not reaction time test. Temperament did not correlate with polygenic score for intelligence and did not modify an association between the polygenic score and cognitive performance, either. High persistence was associated with higher visual memory ( $B = 0.092$ ; FDR-adj.  $p = 0.007$ ) and low harm avoidance with higher overall cognitive performance, specifically better reaction time ( $B = -0.102$ ; FDR-adj.  $p = 0.007$ ). The subscales of harm avoidance had different associations with cognitive performance: higher “anticipatory worry,” higher “fatigability,” and lower “shyness with strangers” were associated with lower cognitive performance, while the role of “fear of uncertainty” was subtest-related. In conclusion, temperament does not help or hinder one from realizing their genetic potential for intelligence. The overall modest relationships between temperament and cognitive performance advise caution if utilizing temperament-related information e.g. in working-life recruitments. Cognitive abilities may be influenced by temperament variables, such as the drive for achievement and anxiety about test performance, but they involve distinct systems of learning and memory.

#### KEYWORDS

CANTAB, cognitive abilities, cognitive performance, cognitive test, genetic, GWAS, intelligence, polygenic score, prospective, TCI, temperament

## 1 | INTRODUCTION

Cognitive abilities such as working memory, episodic memory and sustained attention, are highly heritable, with the estimates of the proportion of inheritance being around 50% or above and increasing toward late adulthood.<sup>1–5</sup> During the last two decades, numerous candidate genes for intelligence have been proposed, but the findings regarding candidate genes have mostly not been replicated.<sup>6,7</sup> Recently, several large-scale genome-wide association studies (GWAS) have enabled a more reliable identification of the polygenic architecture of cognitive abilities<sup>2,8</sup> one of them being based on meta-analysis conducted by Savage and coworkers.<sup>9</sup> This analysis is built on the firmly established concept, originally produced by Spearman,<sup>9,10</sup> that the different aspects of cognitive functioning including verbal and mathematical ability, abstract reasoning, processing speed, executive functioning, spatial reasoning and memory—are considerably captured by a single underlying latent factor, labeled general intelligence or “g.” Still, there is substantial variation between different cognitive aspects in their g-loading.<sup>11</sup> The genome-wide meta-analysis by Savage et al.,<sup>9</sup> combined data from 14 independent cohorts totaling 269,867 participants of European ancestry and 9,295,118 genetic variants associated with cognitive performance in various tests, resulting in the identification of 190 novel loci and 939 novel genes, and replicating previous associations with 15 loci and 77 genes. The resulting polygenic score explained 5.2% of the variance in cognitive performance in four independent samples.<sup>9</sup>

Even though there is considerable evidence supporting the concept of polygenic scores for cognitive ability, they still explain only a minor share of the total variance of cognitive performance,<sup>2,12</sup> because actual performance is likely to be dependent on complex interactions among groups of genes (i.e., epistasis),<sup>13</sup> and on a great variety of factors commonly interacting with genes. Interacting factors include, for example, familial socioeconomic environment, childhood education and environmental cognitive stimulation.<sup>14–17</sup> For example, an interaction between genetic propensity for intelligence and SES on cognitive performance has been reported both from twin<sup>18</sup> and GWAS design studies,<sup>19</sup> even if contradicting findings also exist.<sup>20</sup>

Analogously to the interaction found regarding SES, it possible that temperament might interact with genes and as a result help or hinder the realization of one's genetic intelligence potential. Temperament is a set of early emerging, partially heritable dispositions, which are relatively stable over the lifetime and among other things, describe how an individual reacts to novel stimuli.<sup>21</sup> It has been convincingly showed that individuals are differentially susceptible to the psychosocial environment depending on their temperament.<sup>22–25</sup> Also, one single-gene study has found that temperament may modify an association of genetic factors with academic performance in adulthood.<sup>26</sup> Still, evidence concerning the existence of potential interaction between genes and temperament on cognitive performance is lacking.

The present study was taken with a purpose to examine whether temperament modifies an association between the genetic intelligence potential and performance in cognitive tests in midlife. That is,

we investigated whether there are temperament dimensions that impair or promote realizing the genetic intelligence potential. Existence of such, would be an important discovery warranting implications, for example, considering whether individuals with certain temperament would need support to realize their intelligence potential.

Temperament was assessed in terms of Cloninger's psychobiological theory of personality.<sup>27,28</sup> According to Cloninger et al.,<sup>21</sup> temperament is the "disposition of a person to learn how to behave, react emotionally, and form attachments automatically by associative conditioning." According to Cloninger,<sup>21</sup> in addition to general intelligence, humans have three distinct systems of learning and memory (i.e., associative conditioning, intentionality and self-awareness), which are associated with different components of personality. Associative conditioning (i.e., how we learn to react automatically, including classical and operant conditioning) is the evolutionarily first emerged system and forms the basis for temperament.<sup>28</sup> Further, the associative learning system has been empirically connected with genes having neural functions related to cognitive abilities, including memory and cognitive flexibility.<sup>29</sup>

Cloninger's psychobiological model proposes that there are four temperament dimensions: novelty seeking, harm avoidance, reward dependence and persistence. Novelty Seeking refers to activation behavior and the tendency to approach novel stimuli.<sup>21</sup> Harm Avoidance refers to the tendency to inhibitory behavior in the presence of aversive stimuli. Reward dependence refers to the tendency to respond positively and maintain the behavior in the presence of reward signals, while persistence refers to the tendency to maintain the behavior despite the lack of reward.<sup>21</sup> Although the temperament traits are comparatively stable overage, there are some maturational changes: Persistence typically slightly increases and novelty seeking typically decreases over age.<sup>30</sup>

Temperament might exert its effect in two ways. First, it may have a long-term effect via one's way to react to environmental stimuli: that is, whether one approaches or avoids stimuli that might help to develop cognitive abilities and how one capitalizes on possibilities to learn.<sup>31</sup> In this way, temperament may precede cognitive performance. Second, temperament may have a situation-related (cross-sectional) effect on performance.<sup>32</sup> That is, it may promote<sup>33,34</sup> or impair<sup>35,36</sup> one's test performance as has been widely documented in previous studies. More specifically, temperamental dispositions such as a tendency to be fearful or worried may decrease one's test performance, first, via increased stress and anticipation of failure prior to a cognitive task and, second, via increasing perceived stress and reducing one's ability to concentrate and continue despite fatigue during a task.<sup>32</sup>

Previous cross-sectional studies have shown an association of high persistence and low harm avoidance with higher cognitive performance while reported associations regarding novelty seeking or reward dependence with cognitive performance have been inconclusive.<sup>33,37,38</sup> Additionally, several studies have examined the associations of Big Five personality traits with cognitive performance.<sup>39–41</sup> First, high conscientiousness, which is a trait correlating with high

persistence,<sup>21,42</sup> is found to associate with higher cognitive performance.<sup>40,43–45</sup> Second, high harm avoidance and particularly its subscale of anticipatory worry are known to correlate with high neuroticism<sup>21,42,46</sup> that, in turn, is found to predict lower cognitive performance.<sup>45</sup> However, as far as we know, there is a lack of studies to examine how temperament precedes cognitive performance.

Taken together, we investigated if Cloninger's temperament dimensions are associated with over- or under-realization of polygenic intelligence potential. In addition, we examined both prospective and cross-sectional associations between temperament and test performance; that is, how temperament precedes cognitive performance, and how temperament correlates with cognitive performance cross-sectionally. This study utilized the population-based data of "The Cardiovascular Risk in Young Finns Study" (YFS), where the subjects have been followed over 30 years. This makes possible both cross-sectional and prospective study designs. On the basis of previous literature, we hypothesized that high persistence and low harm avoidance are associated with higher cognitive performance.<sup>33,38</sup> We did not set any hypothesis regarding novelty seeking and reward dependence because previous findings on the topic have been inconclusive. Our investigations regarding interactions between temperament and polygenic intelligence potential were exploratory by nature.

## 2 | MATERIALS AND METHODS

### 2.1 | Participants

The study participants were members of the YFS. They were selected randomly from six birth cohorts (born in 1962, 1965, 1968, 1971, 1974 and 1977) who were living nearby the Finnish universities with medical schools. The sampling was conducted using the Finnish population register of the Social Insurance Institution. The YFS was conducted in accordance with the Declaration of Helsinki, and the ethical committees of all the Finnish universities with medical schools approved the study design at the beginning of the study. A more detailed description of the study population is found elsewhere.<sup>47</sup>

The total sample of the YFS included 3596 participants (ethnic Finns) at the baseline in 1980. For this study, temperament dimensions were assessed four times: in fifth, sixth, seventh and eighth follow-ups of the YFS. That is, in 1997 (participants were 20–35 years old), 2001, 2007, and 2012 (participants were 35–50 years old), enabling prospective examination of the temperament dimensions. Cognitive performance was measured in 2012, and polygenic score for intelligence was calculated after Savage's et al. GWA study<sup>9</sup> on intelligence was published.

We included all the participants with data available on (i) sex and age, (ii) polygenic score for intelligence (PGSI), (iii) at least one domain of cognitive performance and (iv) all the temperament dimensions in at least one measurement year. For each single temperament scale, all the participants with responses for at least 95% of the items were included. Accordingly, the final data in our analyses included 1647 participants.

## 2.2 | Midlife cognitive performance

The cognitive performance of the participants was assessed with the Cambridge Neuropsychological Test Automated Battery (CANTAB), which is a computerized test measuring several cognitive domains.<sup>48</sup> The full CANTAB test battery includes altogether 24 individual tests and has been shown to have good construct validity and discriminant validity.<sup>49,50</sup>

In the current study, we used a test battery with four tests that could be completed in ~20–30 min. Participants completed four tests which were (1) Paired Associates Learning (PAL), (2) Reaction Time (RTI), (3) Rapid Visual Information Processing (RVP) and (4) Spatial Working Memory (SWM). The *Paired Associates Learning* test measured visual episodic memory and visuospatial associative learning. The *Reaction Time* test measured reaction time and response accuracy. The *Rapid Visual Information Processing* test measured sustained visual attention. The *Spatial Working Memory* test measured spatial working memory and the ability to solve problems using self-organized search strategies.<sup>48</sup> A detailed description of the cognitive performance testing procedure has been reported previously.<sup>51</sup>

Each cognitive test produced several outcome variables (e.g., reaction time, number of errors, movement time). A standardized sum variable was calculated for each test by first, transforming each variable into a scale with a mean of 0 and a SD of 1. Then we calculated testwise scores by summing the individual standardized variables within each test and then divided it by the number of variables in that particular test. An overall cognitive performance score was calculated as an average of the testwise sum variables. The calculation of the CANTAB variables is described in more detail elsewhere.<sup>51</sup>

## 2.3 | Polygenic score for intelligence

For each participant, we calculated a polygenic score to reflect their genetic intelligence potential. The genotyping was performed for 2443 samples using a custom build Illumina Human 670 k BeadChip at Wellcome Trust Sanger Institute. Genotypes were called using Illuminus clustering algorithm.<sup>52</sup> Genotype imputation was done using Beagle software<sup>53</sup> and The Sequencing Initiative Suomi (SISu) as reference data. A polygenic score for intelligence was calculated using LDpred, a Bayesian method that estimates posterior mean causal effect sizes from genome wide association (GWA) study summary statistics by assuming a prior for the genetic architecture and linkage disequilibrium (LD) information from a reference panel<sup>54</sup>: an infinitesimal model of causal variants was assumed, and summary statistics from Savage et al.,<sup>9</sup> GWA study for intelligence were used ([https://ctg.cncr.nl/software/summary\\_statistics/](https://ctg.cncr.nl/software/summary_statistics/), see section “Summary statistics for intelligence, wave 2 from Jeanne Savage et al., 2018”). Savage's et al. study identified altogether 205 genomic loci associated with intelligence. The LD between markers was estimated from the SISu data.

The infinitesimal model was selected because it performed the best when evaluating 10 different possibilities (1.0000e+00, p1.0000e-01, 1.0000e-02, 1.0000e-03, 1.0000e-04, 3.0000e-01, 3.0000e-02, 3.0000e-03, 3.0000e-04 and infinitesimal). The selection

was done using YFS data so the model performance might be a slight overestimate as the selection and actual modeling were done in same data set. Computation was carried out using Ubuntu-based virtual machine instance running on Google Cloud Platform. LD radius of 2000 was selected to account for longer LD blocks among Finns compared with other non-Finnish European populations.

A more detailed statistical description of the genetic method is presented here: we had genome-wide SNP data from a custom Illumina BeadChip containing 670,000 SNPs and CNV probes from 2442 YF participants (1123 males, 1319 females). The custom content on the custom 670 K array replaced some poor performing SNPs on the Human610 BeadChip and added more CNV content, and includes 546,677 SNPs passing QC from 594,210 SNPs on the chip. The custom 670 K chip shares 562,643 SNPs in common with the Illumina Human610 BeadChip. Genotypes were called using Illumina's clustering algorithm.<sup>52</sup> A total of 2556 samples were genotyped. After initial clustering, we removed two subjects for poor call rates (CR < 0.90), and 54 samples failed subsequent QC (i.e., duplicated samples, heterozygosity, low call rate, or custom SNP fingerprint genotype discrepancy). The following filters were applied to the remaining data: MAF 0.01, GENO 0.05, MIND 0.05 and HWE  $1 \times 10^{-6}$ . Three of 2500 individuals were removed for low genotyping (MIND >0.05), 11,766 markers were excluded based on HWE test ( $p \leq 1 \times 10^{-6}$ ), 7746 SNPs failed missingness test (GENO >0.05), 34,596 SNPs failed frequency test (MAF < 0.01) and one individual failed gender check. A final list of 546,677 SNPs passed QC and allele frequency filters. For further information, please see Smith et al. study<sup>55</sup>

## 2.4 | Temperament dimensions

Temperament dimensions were measured using the temperament and character inventory (TCI).<sup>56</sup> The TCI includes four temperament dimensions that are novelty seeking, harm avoidance, reward dependence and persistence. The scale of *Novelty Seeking* (NS) consists of 40 statements (e.g., “I do things spontaneously”), *Harm Avoidance* (HA) with 35 statements (e.g., “I avoid meeting strangers”), *Reward Dependence* (RD) with 24 statements (e.g., “I'm strongly moved by sentimental appeals”), and *Persistence* (PS) with eight statements (e.g., “I often push myself to exhaustion”). All the statements were self-rated with a five-point Likert scale ranging from 1 (completely disagree) to 5 (completely agree).

We calculated the average score of the items for each temperament dimension (four dimensions) at each measurement year. The average scores were standardized with the sample mean and SD. We conducted two kinds of analyses: (1) cross-sectional analyses where we examined the associations of temperament dimensions in 2012 with cognitive performance in 2012; and (2) prospective analyses where we examined the associations of temperament dimensions in 1997–2007 with cognitive performance in 2012. In the prospective analyses, we used the average scores of temperament dimensions between measurement years 1997, 2001 and 2007 (i.e., the years preceding cognitive test performance).

The construct validity and test–retest reliability of the TCI temperament scales have been shown to be good in previous studies.<sup>28,30,57–61</sup> In our sample, the temperament scales had good or very good internal reliability for NS (Cronbach's  $\alpha = 0.84$ – $0.85$  between 1997 and 2012), HA ( $\alpha = 0.92$ – $0.93$ ), and RD ( $\alpha = 0.79$ – $0.82$ ), and acceptable internal reliability for PS ( $\alpha = 0.63$ – $0.68$ ). The test–retest correlations between the measurement points were relatively high (ranging between  $r = 0.68$ – $0.86$  for NS,  $r = 0.67$ – $0.84$  for HA,  $r = 0.68$ – $0.82$  for RD, and  $r = 0.50$ – $0.72$  for PS).

## 2.5 | Statistical analyses

We conducted statistical analyses using the RStudio 1.4.17. We examined attrition by comparing the included ( $n = 1647$ ) and excluded ( $n = 1949$ ) participants with regard to study variables (in the comparisons, we included those excluded participants who had data available on each study variable). In attrition analyses, we used independent samples  $t$  tests and chi-squared tests. We conducted multivariate linear regression analyses to examine the associations of PGSI and temperament dimensions with cognitive performance. The statistical requirements (e.g., normality, homoscedasticity) for the linear regression analyses were scrutinized graphically and statistically and found to be met appropriately (for further details, please see Supplementary Methods and Figures S1–S2).

In all analyses, dependent variables included both the overall cognitive performance and the performance in the four cognitive domains of the CANTAB (PAL, RTI, RVP, SWM),<sup>48</sup> given that overall cognitive performance does not capture entirely the variation in different aspects of cognitive performance. The temperament dimensions (NS, HA, RD and PS) were added as the independent variables simultaneously to all analyses. In the cross-sectional analyses, we used temperament dimensions measured in 2012 (i.e., in the same year with cognitive test performance); and in the prospective analyses, we used the average scores of temperament dimensions between measurement years 1997, 2001 and 2007 (i.e., the years preceding cognitive test performance). First, we investigated whether temperament dimensions are associated with cognitive performance when controlling the PGSI. Thus, the temperament dimensions and PGSI were set as independent variables. Next, we investigated whether the temperament dimensions modify the association between the PGSI and cognitive performance. Hence, in that analysis we also included all the two-way interaction effects between PGSI, each temperament dimension and control variables, as has been recommended previously.<sup>62</sup>

That is, we examined whether participants scoring high on a certain temperament dimension, such as HA, would have higher cognitive performance if polygenic score for intelligence is high, whereas they would have low cognitive performance if polygenic score for intelligence is low. In all the analyses, control variables included sex, age, and the 10 first ancestrally informative principal components. The principal components were calculated before the polygenic score calculation, and they were estimated using quality-controlled GWAS chip data (the principal components were calculated with Plink software by using Plink's—pca command).

For the variance explained by each independent variable, we calculated the adjusted  $R$  squared when separately adding the independent variable in question to the model (including also the covariates and the other independent variables). Because multiple analyses were done, we applied false discovery rate-correction (FDR),<sup>63</sup> and all the reported  $p$ -values are FDR-corrected unless otherwise stated. FDR correction was applied to all  $p$ -values of variables with hypothesized main effects or interactions (i.e., PGSI, temperament and their interaction variables for interaction analyses, and PGSI and temperament variables for the other analyses) calculated in one model/analysis simultaneously. For example, when examining the interactions between temperament traits in 2012 and cognitive performance (Table 3, the right column), altogether  $9 \times 5 = 45$   $p$ -values were calculated (9 [PGSI, four temperament traits, and four interactions between PGSI and temperament traits]  $\times 5$  [five cognitive outcome variables] = 45  $p$ -values). All those  $p$ -values were simultaneously FDR-corrected, while  $p$ -values of the control variables were not FDR-corrected.

## 3 | RESULTS

The descriptive statistics of the study variables are presented in Table 1. The mean age of the included participants was 42.9 (range 35–50) years at the time of the cognitive performance measurement. Fifty-six percent of the participants were female.

The attrition analyses showed that the included participants (56% female) were older (42.9 vs. 42.1, unadjusted  $p < 0.001$ ) and performance in the overall cognition (0.02 vs.  $-0.1$ ,  $p = 0.038$ ) and sustained attention test (0.02 vs.  $-0.09$ , unadjusted  $p = 0.049$ ) than those not included. There was no attrition bias in PGSI, visual memory, reaction time or working memory tests. Regarding temperament dimensions, the included participants had lower NS ( $-0.08$  vs. 0.11, unadjusted  $p < 0.001$ ), lower HA ( $-0.03$  vs. 0.05, unadjusted  $p = 0.034$ ) and higher RD (0.05 vs.  $-0.07$ ; unadjusted  $p = 0.003$ ) than the participants not included. In there was no attrition bias.

Table 2 presents the results of linear regression analyses when predicting cognitive performance by PGSI and temperament dimensions. The PGSI was significantly associated with the overall cognitive performance and performance in visual memory, sustained attention and working memory tests but not reaction time test. Our additional analyses showed that the PGSI independently explained 2.3%, 1.5%, 2.0% and 0.8% of the variation in overall cognitive performance, visual memory, sustained attention test and working memory test, respectively. Further, there were no significant associations between PGSI and any of the four temperament dimensions.

As shown in Table 2, low HA was prospectively and cross-sectionally associated with higher overall cognitive performance ( $B = -0.080$ ;  $p = 0.025$  and  $B = -0.076$ ;  $p = 0.034$ , respectively) and higher performance in reaction time ( $B = -0.097$ ;  $p = 0.009$  and  $B = -0.102$ ;  $p = 0.007$ , respectively). In addition, high PS was cross-sectionally associated with higher performance in visual memory ( $B = 0.092$ ;  $p = 0.007$ ), whereas RD and NS had no significant associations with cognitive performance.



	Mean/frequency (%)	SD	Range
Age	42.90	5.02	35; 50
Sex (female)	923 (56.0)		
Polygenic score for intelligence	0.02	1.01	-2.75; 3.33
Temperament dimensions			
Novelty seeking	-0.08	0.98	-4.00; 3.82
Harm avoidance	-0.03	0.95	-2.68; 4.05
Reward dependence	0.05	0.97	-4.09; 2.57
Persistence	0.02	0.98	-3.30; 3.30
Cognitive performance			
Overall	0.02	0.99	-2.36; 2.62
PAL	0.01	0.99	-3.40; 1.91
RTI	0.01	0.99	-3.17; 2.30
RVP	0.02	1.00	-2.20; 3.01
SWM	0.01	0.99	-3.42; 2.12

**TABLE 1** Descriptive statistics of the study variables

Note:  $n = 1647$ .

Abbreviations: PAL, paired associates learning; RTI, reaction time; RVP, rapid visual information processing; SWM, spatial working memory.

As additional analyses, we reran the models without including the PGSI as a covariate and present the results in Table S2. Overall, all the significant associations between temperament and cognitive performance remained, and some of the associations seemed to become slightly stronger.

As shown in Table 3, no significant interactions emerged between temperament and PGSI (a more detailed table of the results regarding covariates is provided in Table S3).

HA independently explained 0.9% of the reaction time and Persistence independently 0.8% of the visual memory performance. Thus, hypothetically, two individuals would differ by  $\sim 0.42$  SD in their reaction time performance and  $\sim 0.37$  SD by visual memory depending on their HA and PS being high versus low ( $\pm 2$  SD).

As additional analyses, we examined whether the subscales of HA were associated with cognitive performance (i.e., the only temperament dimension with significant effects on cognitive performance and with subscales) when entered into the analysis together with the PGSI. The results of regression analysis are shown in Table S1. To summarize the findings, all four HA's subscales (viz., low "anticipatory worry," high "fear of uncertainty," low "fatigability," and high "shyness with strangers") had associations with higher cognitive performance. Specifically, low "anticipatory worry" was associated prospectively and cross-sectionally with higher visual memory ( $B = -0.115$ ;  $p = 0.016$  and  $B = -0.110$ ;  $p = 0.020$ , respectively), sustained attention ( $B = -0.096$ ;  $p = 0.041$  and  $B = -0.100$ ;  $p = 0.049$ , respectively) and overall cognitive performance ( $B = -0.104$ ;  $p = 0.022$  and  $B = -0.123$ ;  $p = 0.008$ , respectively), and prospectively with higher working memory ( $B = -0.093$ ;  $p = 0.041$ ). High "Fear of Uncertainty" was cross-sectionally associated with higher sustained attention performance ( $B = 0.162$ ;  $p < 0.001$ ), but prospectively with lower visual memory ( $B = -0.088$ ;  $p = 0.038$ ) and working memory ( $B = -0.084$ ;  $p = 0.043$ ). High

"Shyness with Strangers" was prospectively and cross-sectionally associated with higher visual memory ( $B = 0.107$ ;  $p = 0.010$  and  $B = 0.098$ ;  $p = 0.029$ , respectively) and prospectively with higher working memory ( $B = 0.095$ ;  $p = 0.021$ ) and overall cognitive performance ( $B = 0.083$ ;  $p = 0.038$ ). High "Fatigability" was prospectively related to lower reaction time performance ( $B = -0.103$ ;  $p = 0.021$ ) and cross-sectionally with lower sustained attention ( $B = -0.113$ ;  $p = 0.014$ ). We also reran these analyses without PGSI as covariate (see Table S4).

## 4 | DISCUSSION

Our results indicated that temperament was not related to the suggested genetic background of intelligence potential, and did not modify an association between the polygenic score for intelligence and cognitive performance, either. No significant interaction between the PGSI and temperament dimension survived after the correction for multiple testing. The findings of the current study suggest that a role of temperament in cognitive performance is equal at each level of the polygenic score for intelligence. This means that no temperament dimension seems to give extra advantage or hindrance to an individual's cognitive performance, be their genetic intelligence potential high or low. In other words, temperament does not put individuals on advantaged or disadvantaged position in realizing their potential, in contrast what has been found in regards certain environmental factors (e.g., socioeconomic status) that have been reported modify the realization of genetic intelligence potential.<sup>18,64</sup> Importantly, we see two other potential explanations for the lack of significant interactions. First, as it is proposed that temperament should be also analyzed as combinations of dimensions, that is, temperament profiles,<sup>21,65</sup> it cannot be ruled out that the potential interaction emerges at

**TABLE 2** Results of regression analyses, when examining the main effects of temperament dimensions and polygenic score for intelligence on performance in cognitive tests (measured with CANTAB)

	Temperament dimensions in 1997–2007				Temperament dimensions in 2012			
	<i>B</i>	95% CI	<i>p</i>	FDR-adj. <i>p</i>	<i>B</i>	95% CI	<i>p</i>	FDR-adj. <i>p</i>
Overall cognitive performance								
PGSI	<b>0.181</b>	<b>0.133; 0.229</b>	<b>&lt;0.001</b>	<b>&lt;0.001</b>	<b>0.150</b>	<b>0.096; 0.204</b>	<b>&lt;0.001</b>	<b>&lt;0.001</b>
Novelty seeking	0.017	−0.037; 0.071	0.527	0.770	−0.008	−0.065; 0.049	0.788	0.895
Harm avoidance	<b>−0.080</b>	<b>−0.137; −0.023</b>	<b>0.006</b>	<b>0.025</b>	<b>−0.076</b>	<b>−0.134; −0.018</b>	<b>0.010</b>	<b>0.034</b>
Reward dependence	0.010	−0.046; 0.066	0.733	0.942	0.016	−0.044; 0.076	0.606	0.783
Persistence	0.029	−0.022; 0.080	0.270	0.520	0.054	−0.001; 0.109	0.055	0.154
PAL score								
PGSI	<b>0.133</b>	<b>0.085; 0.181</b>	<b>&lt;0.001</b>	<b>&lt;0.001</b>	<b>0.123</b>	<b>0.068; 0.178</b>	<b>&lt;0.001</b>	<b>&lt;0.001</b>
Novelty seeking	−0.006	−0.060; 0.048	0.829	0.942	−0.037	−0.095; 0.021	0.205	0.397
Harm avoidance	−0.038	−0.095; 0.019	0.191	0.435	−0.050	−0.108; 0.008	0.094	0.234
Reward dependence	−0.026	−0.083; 0.031	0.365	0.608	−0.026	−0.087; 0.035	0.403	0.638
Persistence	0.055	0.003; 0.107	0.039	0.123	<b>0.092</b>	<b>0.036; 0.148</b>	<b>0.001</b>	<b>0.007</b>
RTI score								
PGSI	0.015	−0.036; 0.066	0.555	0.770	0.025	−0.034; 0.084	0.408	0.638
Novelty seeking	−0.034	−0.091; 0.023	0.248	0.517	−0.019	−0.080; 0.042	0.549	0.762
Harm avoidance	<b>−0.097</b>	<b>−0.157; −0.037</b>	<b>0.002</b>	<b>0.009</b>	<b>−0.102</b>	<b>−0.164; −0.040</b>	<b>0.001</b>	<b>0.007</b>
Reward dependence	0.069	0.009; 0.129	0.024	0.086	0.069	0.004; 0.134	0.038	0.117
Persistence	0.003	−0.052; 0.058	0.904	0.942	−0.022	−0.082; 0.038	0.473	0.696
RVP score								
PGSI	<b>0.186</b>	<b>0.135; 0.237</b>	<b>&lt;0.001</b>	<b>&lt;0.001</b>	<b>0.144</b>	<b>0.084; 0.204</b>	<b>&lt;0.001</b>	<b>&lt;0.001</b>
Novelty seeking	0.024	−0.033; 0.081	0.418	0.654	−0.005	−0.067; 0.057	0.883	0.948
Harm avoidance	−0.045	−0.106; 0.016	0.150	0.376	−0.041	−0.104; 0.022	0.207	0.397
Reward dependence	0.005	−0.055; 0.065	0.878	0.942	0.004	−0.062; 0.070	0.910	0.948
Persistence	−0.002	−0.057; 0.053	0.953	0.953	0.014	−0.047; 0.075	0.662	0.788
SWM score								
PGSI	<b>0.104</b>	<b>0.055; 0.153</b>	<b>&lt;0.001</b>	<b>&lt;0.001</b>	<b>0.087</b>	<b>0.031; 0.143</b>	<b>0.002</b>	<b>0.010</b>
Novelty seeking	0.028	−0.027; 0.083	0.318	0.568	0.014	−0.044; 0.072	0.627	0.783
Harm avoidance	−0.048	−0.106; 0.010	0.108	0.299	−0.041	−0.100; 0.018	0.173	0.394
Reward dependence	−0.007	−0.064; 0.050	0.805	0.942	0.000	−0.062; 0.062	0.994	0.994
Persistence	−0.006	−0.058; 0.046	0.835	0.942	0.031	−0.026; 0.088	0.291	0.520

Note: Multivariate regression models created to simultaneously predict overall cognitive performance and performance in each of the four CANTAB tests. Covariates included sex and age and 10 first ancestrally informative principal components. FDR-adj. *p* refers to *p*-values adjusted with FDR correction. *B* = unstandardized regression coefficient, that is, how many SDs cognitive performance changes, according to the regression model, with one SD change in a temperament trait or PGSI. CI = 95% confidence interval. Results with FDR-adj. *p* < .05 are in bold.

Abbreviations: PGSI, polygenic score for intelligence; PAL, paired associates learning; RTI, reaction time. RVP, rapid visual information processing. SWM, spatial working memory.

temperament profile level instead of dimension level. Second, although we had a fairly large sample, our sample may still have been underpowered for obtaining statistically significant interactions between the PGSI and temperament. It has been discussed that interaction analyses generally require larger sample sizes than main effect analyses to reach appropriate statistical power and, therefore, gene–environment interactions in samples with limited size should be treated with caution.<sup>66</sup>

Temperament correlated with cognitive performance, as widely documented in previous literature, too.<sup>33,38,67</sup> High Persistence and

low harm avoidance were related to a higher cognitive performance. The effects of temperament on cognitive performance were not strong but still of some significance: for instance, individuals at different levels of persistence or harm avoidance would differ by ~0.37 and ~0.44 SD in their cognitive performance, respectively.

In the light of previous literature<sup>33,34,38</sup> and Cloninger's theory,<sup>28</sup> an association between high persistence and cognitive performance was expected. Persistence is characterized by ambitious, conscientious and determined behavior,<sup>31</sup> which is thought to enhance cognitive performance via lower likelihood for giving up and stronger

**TABLE 3** Results of regression analyses, when predicting cognitive performance by polygenic score for cognitive performance and temperament dimensions

	Temperament dimensions in 1997–2007				Temperament dimensions in 2012			
	B	95% CI	<i>p</i>	FDR-adj. <i>p</i>	B	95% CI	<i>p</i>	FDR-adj. <i>p</i>
Overall cognitive performance								
PGSI	0.137	−0.328; 0.602	0.565	0.804	−0.073	−0.585; 0.439	0.780	0.966
Novelty seeking	0.408	−0.066; 0.882	0.091	0.480	0.211	−0.290; 0.712	0.410	0.939
Harm avoidance	0.274	−0.248; 0.796	0.303	0.758	0.217	−0.315; 0.749	0.424	0.939
Reward dependence	−0.311	−0.780; 0.158	0.194	0.623	−0.152	−0.648; 0.344	0.549	0.966
Persistence	0.009	−0.446; 0.464	0.968	0.990	−0.332	−0.830; 0.166	0.191	0.939
PGSI*NS	−0.050	−0.105; 0.005	0.080	0.480	0.002	−0.055; 0.059	0.940	0.966
PGSI*HA	0.021	−0.037; 0.079	0.473	0.804	0.026	−0.032; 0.084	0.375	0.939
PGSI*RD	−0.022	−0.077; 0.033	0.430	0.804	−0.037	−0.098; 0.024	0.239	0.939
PGSI*PS	0.043	−0.010; 0.096	0.107	0.480	0.005	−0.051; 0.061	0.851	0.966
PAL score								
PGSI	−0.013	−0.480; 0.454	0.955	0.990	−0.237	−0.754; 0.280	0.370	0.939
Novelty seeking	0.612	0.136; 1.088	0.012	0.470	0.095	−0.411; 0.601	0.714	0.966
Harm avoidance	0.558	0.034; 1.082	0.037	0.470	0.445	−0.092; 0.982	0.105	0.939
Reward dependence	−0.375	−0.846; 0.096	0.120	0.490	−0.149	−0.650; 0.352	0.560	0.966
Persistence	0.313	−0.144; 0.770	0.180	0.623	0.011	−0.492; 0.514	0.966	0.966
PGSI*NS	−0.053	−0.109; 0.003	0.063	0.470	−0.009	−0.067; 0.049	0.767	0.966
PGSI*HA	0.049	−0.009; 0.107	0.098	0.480	0.049	−0.009; 0.107	0.101	0.939
PGSI*RD	−0.054	−0.109; 0.001	0.054	0.470	−0.090	−0.152; −0.028	0.005	0.203
PGSI*PS	0.052	−0.001; 0.105	0.055	0.470	0.027	−0.030; 0.084	0.355	0.939
RTI score								
PGSI	−0.015	−0.511; 0.481	0.953	0.990	−0.254	−0.811; 0.303	0.371	0.939
Novelty seeking	0.091	−0.414; 0.596	0.723	0.862	0.123	−0.421; 0.667	0.659	0.966
Harm avoidance	−0.175	−0.732; 0.382	0.539	0.804	−0.233	−0.811; 0.345	0.430	0.939
Reward dependence	−0.138	−0.639; 0.363	0.590	0.804	0.293	−0.246; 0.832	0.287	0.939
Persistence	−0.169	−0.654; 0.316	0.495	0.804	−0.055	−0.596; 0.486	0.843	0.966
PGSI*NS	−0.017	−0.076; 0.042	0.582	0.804	0.002	−0.060; 0.064	0.949	0.966
PGSI*HA	0.010	−0.052; 0.072	0.746	0.862	0.017	−0.046; 0.080	0.605	0.966
PGSI*RD	−0.021	−0.079; 0.037	0.473	0.804	0.026	−0.041; 0.093	0.438	0.939
PGSI*PS	0.026	−0.030; 0.082	0.372	0.796	0.005	−0.056; 0.066	0.883	0.966
RVP score								
PGSI	0.501	0.005; 0.997	0.048	0.470	0.509	−0.054; 1.072	0.077	0.939
Novelty seeking	0.040	−0.466; 0.546	0.876	0.962	−0.098	−0.649; 0.453	0.727	0.966
Harm avoidance	0.192	−0.365; 0.749	0.499	0.804	−0.107	−0.692; 0.478	0.719	0.966
Reward dependence	0.104	−0.397; 0.605	0.685	0.856	−0.183	−0.728; 0.362	0.511	0.966
Persistence	0.302	−0.183; 0.787	0.223	0.653	−0.386	−0.933; 0.161	0.167	0.939
PGSI*NS	−0.016	−0.075; 0.043	0.606	0.804	0.004	−0.059; 0.067	0.903	0.966
PGSI*HA	0.029	−0.033; 0.091	0.349	0.786	0.010	−0.054; 0.074	0.759	0.966
PGSI*RD	0.010	−0.048; 0.068	0.747	0.862	−0.019	−0.086; 0.048	0.590	0.966
PGSI*PS	0.028	−0.028; 0.084	0.337	0.786	−0.022	−0.084; 0.040	0.483	0.966
SWM score								
PGSI	−0.133	−0.609; 0.343	0.584	0.804	−0.162	−0.690; 0.366	0.547	0.966
Novelty seeking	0.275	−0.210; 0.760	0.267	0.707	0.364	−0.152; 0.880	0.167	0.939
Harm avoidance	0.326	−0.208; 0.860	0.232	0.653	0.509	−0.039; 1.057	0.069	0.939



TABLE 3 (Continued)

	Temperament dimensions in 1997–2007				Temperament dimensions in 2012			
	B	95% CI	<i>p</i>	FDR-adj. <i>p</i>	B	95% CI	<i>p</i>	FDR-adj. <i>p</i>
Reward dependence	−0.366	−0.847; 0.115	0.135	0.507	−0.257	−0.768; 0.254	0.325	0.939
Persistence	0.001	−0.465; 0.467	0.997	0.997	−0.054	−0.566; 0.458	0.837	0.966
PGSI*NS	−0.015	−0.072; 0.042	0.608	0.804	0.034	−0.025; 0.093	0.256	0.939
PGSI*HA	−0.014	−0.073; 0.045	0.646	0.830	0.003	−0.056; 0.062	0.932	0.966
PGSI*RD	−0.005	−0.061; 0.051	0.871	0.962	−0.030	−0.093; 0.033	0.349	0.939
PGSI*PS	0.016	−0.038; 0.070	0.567	0.804	0.006	−0.052; 0.064	0.831	0.966

Note: Multivariate regression models created to simultaneously predict overall cognitive performance and performance in each of the four CANTAB tests. Covariates included sex and age and 10 first ancestrally informative principal components. FDR-adj. *p* refers to *p* values adjusted with FDR correction. *B* = unstandardized regression coefficient, that is, how many SDs cognitive performance changes, according to the regression model, with one SD change in a temperament trait or PGSI. CI = 95% confidence interval.

Abbreviations: PAL, paired associates learning; PGSI, polygenic score for intelligence; RTI, reaction time; RVP, rapid visual information processing; SWM, spatial working memory.

disposition to concentrate on the task and to strive to perform at one's best.<sup>31,34</sup> In the current study, an association was found only with performance in visual memory and associative learning. This is, however, in accordance with Cloninger's theory where temperament refers to the differences in associative and nonverbal learning and memory.<sup>27</sup>

An association between Persistence and cognitive performance was found only with the 2012 measurement and not with the 1997–2007. In addition to an imperfect stability of temperament across time, this might suggest a more contemporary effect of persistence. That is, high persistence may be related to better cognitive performance in a test situation (e.g., overcoming challenges in a test situation) instead of having a major role in the long-term development of cognitive performance. A temporary effect of persistence has been previously documented at least in a Finnish experimental study,<sup>32</sup> and in a sample of violent offenders,<sup>38</sup> and adolescents.<sup>33,67,68</sup> Interestingly, however, although persistence may only temporarily promote cognitive test performance, it may prospectively enhance higher educational attainments.<sup>69</sup> That is, high Persistence may enable long-term utilization of one's cognitive abilities in practice, in order to reach higher educational goals.

We found that low Harm Avoidance was associated with higher cognitive performance both cross-sectionally and prospectively. In addition, these findings are consistent with Cloninger's theory,<sup>27</sup> proposing that high Harm Avoidance individuals express high anxiety and inhibition when facing novel and unfamiliar tasks, and suggest that in addition to contemporary challenges, this tendency might impair a development of cognitive abilities, too. Further, high Harm Avoidance was especially associated with lower performance in reaction time test. This is in accordance with previous findings: reaction time tests represent aversive stimuli that are perceived as threatening in individuals with high Harm Avoidance, which, in turn, may result in lower test performance.<sup>32</sup>

Although a high harm avoidance has been as a rule associated with a low cognitive performance, conflicting findings have been reported, too.<sup>38,67</sup> Our subscale analysis might clarify that issue. We

found, specifically, that different subscales played contradictory roles: two of them operating in concordance with the total harm avoidance and having an impairing effect on performance, while two other subscales played opposite roles.

High “anticipatory worry” (HA1) and high “fatigability” (HA4) were cross-sectionally associated with and prospectively preceded a lower cognitive performance in different cognitive tests which is plausible as individuals high on these subscales are prone to be anxious, become tired quickly, and give up easier in straining tasks.<sup>56</sup> These tendencies may manifest in a test situation as higher test anxiety that, in turn, associates with lower test performance.<sup>35,36,70</sup> In addition, individuals with high Harm Avoidance are prone to have lower performance appraisal and to anticipate failure,<sup>32</sup> that may impair their ability to do their best.

A role of “fear of uncertainty” (HA2) was slightly complicated: it preceded a lower performance in a visual and a working memory test but a higher one in a sustained attention test. Although apparently mutually contradicting, these findings are not in a conflict with previous literature: feelings of uncertainty and acute stress are suggested to be associated with enhanced attention,<sup>71</sup> but with lower memory performance,<sup>72</sup> and altered functioning of some memory-related brain regions such as the hippocampus.<sup>73</sup> This is in accordance with evolutionary meaningful postulations that high arousal may transfer resources from working memory network to selective attention in order to be able to respond to acutely relevant information.<sup>74</sup>

Our finding that high “shyness with strangers” (HA3) was associated with higher cognitive performance is inconsistent with some previous findings on children,<sup>75,76</sup> but congruent, for instance, with some findings in adolescents regarding academic performance.<sup>67</sup> Further, our finding does not completely disagree with Cloninger's theory, where “shyness” refers to inhibition in social interactions, not necessarily to cognitive challenges.<sup>56</sup>

Finally, we found that novelty seeking and reward dependence played no role in cognitive performance. For reward dependence, previous studies have found a marginal or no effect on cognitive performance,<sup>33,37,38</sup> but a positive effect on educational attainment.<sup>69</sup>

The findings on novelty seeking, in turn, are in accordance with two previous studies reporting no association between Novelty Seeking and cognitive performance.<sup>32,33</sup>

To the best of our knowledge, this study was the first to examine the role of temperament in the realization of genetic intelligence potential in actual cognitive performance. Our findings are in accordance with studies investigating how big five personality traits precede cognitive performance.<sup>39–41</sup> First, high conscientiousness, which is a trait correlating with high persistence,<sup>21,42</sup> is found to associate with higher cognitive performance.<sup>40,43–45</sup> Second, high Harm Avoidance and particularly its subscale of anticipatory worry are known to correlate with high Neuroticism<sup>21,42,46</sup> that, in turn, is found to predict lower cognitive performance.<sup>45</sup>

This study had several strengths. First, instead of a few candidate genes, we used a well-established polygenic score as an indicator of genetic capacity. Second, contrary to previous studies mostly based on relatively small, often clinical samples, we utilized a population based sample. Third, our design enables to examine both prospective and cross-sectional associations. Fourth, unlike many previous studies focusing on children and adolescents, the participants were of optimal age, in their middle adulthood with fully developed cognitive abilities but before any substantial decline in the performance starting typically from late adulthood.<sup>77</sup>

Regarding attrition, the difference in most of the variables between participants included versus excluded from the analyses was insignificant or relatively small. Most significant attrition was obtained in age (included participants were 0.8 years older), sustained attention (included had 0.11 higher score), and Novelty Seeking (included had 0.19 lower score). Overall, attrition bias was comparatively small by effect size (e.g., a 0.8-year difference in age) and may not likely have had any major influence on our results.

The limitations of this study also suggest further lines for upcoming research. First, the polygenic score for intelligence itself possesses notable limitations. The PGSI was significantly associated with the overall cognitive performance and performance in visual memory, sustained attention, and working memory tests but not reaction time test. Even if the score used in this study is based on a recent and major GWAS,<sup>9</sup> it captures only a minority of genetically explainable variation in cognitive performance and does not address the variance from rare or uncommon variants, similarly to most of the polygenic scores.<sup>2,78</sup> In our sample, the PGSI independently explained 2.3%, 1.5%, 2.0% and 0.8% of the variation in overall cognitive performance, visual memory, sustained attention test, and working memory test, respectively. Second, the scales of CANTAB adopted here do not give a comprehensive view on all cognitive domains as they did not include verbal tasks, for example. There appears to be comparatively separate neural systems for encoding verbal and nonverbal information in working memory.<sup>79</sup> Further, completion of the test battery took ~20–30 min and, thus, the findings cannot be directly generalized into tasks requiring concentration over hours. Third, as the baseline CANTAB scores were not available, any firm conclusions about temporal relationships between temperament and cognitive performance cannot be established. Nevertheless, there is evidence that cognitive abilities remain quite stable in middle adulthood: strongest (but still rather

modest) changes appear to occur in processing speed and verbal abilities,<sup>80,81</sup> but those abilities were not measured in this study.

In conclusion, we found that temperament had a modest association with cognitive performance, but it did not have a role in realization of one's intelligence potential. In addition, some associations between temperament and cognition were contradictory to some general suppositions (e.g., the relationship of high shyness with higher cognitive performance). This suggests that it should be carefully considered if aiming to utilize information about temperament traits in recruitment or academic evaluations. Moreover, the findings together with previous evidence indicate that a same cognitive task may induce different threat perceptions, anticipated performance levels and experienced stress levels in individuals with different temperaments. Taken together, the expression and development of cognitive abilities may be influenced by temperament variables, such as the drive for achievement and anxiety about test performance, but they involve distinct systems of learning and memory.

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## CONFLICT OF INTEREST

The author declares that there is no conflict of interest.

## DATA AVAILABILITY STATEMENT

The data sets presented in this article are not readily available because YFS is an ongoing follow-up study and the datasets are not anonymized, and the GDPR prevents public sharing of the data. Instead, pseudonymized data sets are possible to share on request, and requires a data-sharing agreement between the parties. Requests to access the datasets should be directed to Katri Räikkönen (katri.raikkonen@helsinki.fi) or Niklas Ravaja (niklas.ravaja@helsinki.fi) for psychological data set, to Terho Lehtimäki (terho.lehtimaki@tuni.fi) for genetic data set, and to Suvi Rovio (suvrov@utu.fi) for CANTAB data set.

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