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Polygenic risk for schizophrenia predicting Big Five personality traits in individuals without non-affective psychosis

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ABSTRACT

Background: A high genetic risk for schizophrenia, in complex interplay with environmental factors, has been suggested to explain population-level variation in personality traits among individuals who do not develop schizophrenia-spectrum disorders. We investigated, first, whether polygenic risk for schizophrenia (PRSscz) predicts Big Five personality traits in individuals, who have not developed non-affective psychosis. Second, we examined whether any observed associations are specific to PRSscz or evident also for PRS for major depression (PRS_{DEP}).

Study design: The participants came from the population-based, prospective Young Finns Study (n = 1328–1874 in the final analyses). Diagnoses of non-affective psychoses were obtained from the Finnish hospital care register. Personality traits were assessed with the five-factor model including Neuroticism, Conscientiousness, Openness, Agreeableness, and Extraversion. Covariates included age, sex, adulthood educational level, and quality of early family environment (adverse socioeconomic circumstances, unfavorable emotional family atmosphere, and stressful life events).

Results: In those without non-affective psychosis, PRSscz had a positive linear effect on Openness (B = 0.029, 95%CI = 0.006;0.052, p = 0.014) and a quadratic effect on Extraversion (B = -0.018, 95%CI = -0.033;-0.002, p = 0.024), indicating higher levels of Extraversion in those with low/high levels of PRSscz. The PRSscz did not account for other personality traits. The results held after adding covariates or after controlling for PRS_{DEP}. PRS_{DEP} was not associated with any of the personality traits.

Conclusions: Individuals with high PRS for schizophrenia, who have not developed non-affective psychosis, may still develop mildly different personality traits, including higher Openness and lower Extraversion. These findings seem to be specific to PRSscz and are not observed for PRS_{DEP}.

1. Introduction

Schizophrenia is a chronic and severe mental disorder characterized by disturbances in thought, perception, emotion, and social functioning (American Psychiatric Association, 2022). More recent conceptualizations view schizophrenia as an umbrella term covering heterogeneous manifestations of hallucinations, delusions, disorganized thinking and behavior, and impairments in cognitive performance (Guloksuz and van

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Os, 2018).

Previous twin studies have demonstrated that schizophrenia has a strong genetic component, with estimated heritability of around 80 % (Hilker et al., 2018; Sullivan et al., 2003). Genome wide association (GWA) studies are one of the latest methods of assessing genetic predisposition to schizophrenia. GWA-studies consist of sampling a representative part of the human genome and regressing the prevalence of the single nucleotide polymorphisms to an outcome of interest, such as schizophrenia diagnosis (Uffelmann et al., 2021). In GWA studies, large reference samples are needed to have power to detect contributing variants (Bogdan et al., 2018). To date, schizophrenia has been established as highly polygenic disorder with thousands of genes, along with cases of rare variants contributing to its manifestation (Trifu et al., 2020). The most recent published GWA-study concerning schizophrenia (incl. 76,755 schizophrenia patients and 243,649 controls) identified 287 loci associated with the outcome of schizophrenia diagnosis (Trubetskoy et al., 2022). Polygenic risk scores for schizophrenia (PRS_{SCZ}), calculated based on the results of GWA studies, consist of a weighted sum of risk alleles. The PRSscz largely captures common low penetrance variants which occur in a significant portion of the population (<5 %), but it does not include copy number variants contributing to the disorder (Marshall et al., 2017; Owen et al., 2023). PRS_{SCZ}s typically explain 2–7 % of the liability to the disorder when combined into a polygenic risk score (Owen et al., 2023; Trubetskoy et al., 2022). In recent years, there has been growing interest in examining alternative outcomes of polygenic risk for schizophrenia, such as personality.

The dimensional liability model of schizophrenia-spectrum psychopathology (Guloksuz and van Os, 2018) provides a framework for investigating the associations of PRS_{SCZ} and personality. According to the model, schizophrenia represents an extreme end of an aetiopathophysiological continuum of liability to schizophrenia-spectrum psychopathology (Guloksuz and van Os, 2018). Milder manifestations of the continuum include less chronic, less functionally impairing, and less pathological forms of schizotypal thinking and behavior. Schizotypy represents dimensions of personality that, in part, index genetic risk for developing schizophrenia-spectrum disorders. Psychometric studies on schizotypy have idenfitied three distinct dimensions: positive, negative, and disorganized schizotypy (Barrantes-Vidal et al., 2015). In sum, this liability framework suggests that, in complex interactions with environmental exposures, the genetic load for schizophrenia may manifest milder personality-related variation (i.e., schizotypal traits) among those who do not develop schizophrenia or related disorders (Lenzenweger, 2023).

Regarding previous evidence, studies have reported associations of PRS_{SCZ} with positive state-like schizotypal dimension (Meller et al., 2025), associations with two out of nine schizotypy subdimensions, namely delusional experiences and reduced social engagement (Tiego et al., 2023), and no associations (Nenadić et al., 2022). Additionally, PRS_{SCZ} has not associated with clinical personality measures, such as callous-unemotional traits, grandiosity, or paranoid ideation in adolescents (Krapohl et al., 2016). In sum, while the results of previous studies have suggested associations of PRS_{SCZ} with varying subdimensions of schizotypal traits, the effects of PRS_{SCZ} on normal personality traits have remained less investigated.

The most widely used model of normal personality traits is the Five-Factor model of personality ("Big Five"), which describes individual differences in dispositions to behave, think, and feel across situations and includes five traits: Openness, Conscientiousness, Extraversion, Agreeableness and Neuroticism (McCrae and John, 1992). Several Big Five traits have been previously proposed to be connected to schizotypal traits. In a previous study negative symptoms were significantly predicted by high Neuroticism, and low Extraversion, Openness, and Agreeableness (Ross et al., 2002). Positive symptoms were associated with high Neuroticism and Openness, and low Agreeableness (Ross et al., 2002). Furthermore, items measuring Openness to experience have been found to form a common factor with items from measures of positive schizotypy (Straub and Kerns, 2025). To the best of our knowledge, only one previous study has examined the associations between PRS_{SCZ} and Big Five personality traits in the UK among 15-year-old adolescents, reporting null results (Krapohl et al., 2016). However, there is evidence that many Big Five personality traits show temporary dips in adolescence (around ages 16–17 years) (Borghuis et al., 2017), raising the question of whether the null results might be influenced by the age of the UK sample and highlighting the importance of studying adult samples.

We investigated whether polygenic risk for schizophrenia is associated with Big Five personality traits in individuals who have not developed non-affective psychosis. Second, we examined whether any observed associations are specific to polygenic risk for schizophrenia or evident also for polygenic risk for major depression. We used data from the Young Finns Study which is a population-based cohort study with a five-year follow-up of personality traits. Polygenic risk for schizophrenia and major depression were assessed on the basis of the latest GWA-studies (Howard et al., 2019; Trubetskoy et al., 2022).

2. Methods

2.1. Participants

The participants came from the Young Finns Study (YFS), which is an ongoing prospective follow-up study. The YFS started in 1980, and the participants have been followed regularly since then. The sampling was designed to include a population-based sample of non-institutionalized Finnish children, representative with regard to sex (male vs. female), rural vs. urban environment, and Eastern vs. Western regions in Finland. The sample consisted of six age cohorts (born in 1962, 1965, 1968, 1971, 1974, or 1977). Altogether 4320 subjects were invited, and 3596 of them participated in the baseline study. The design of the YFS is described with further details elsewhere (Akerblom et al., 1985; Raitakari et al., 2008).

The YFS has been carried out in accordance with the Declaration of Helsinki, and the study design has been approved by the ethical committees of all Finnish Universities with a medical faculty (Universities of Helsinki, Turku, Tampere, Kuopio, and Oulu). All the participants or their parents (participants aged <18 years) provided informed consent before participation.

Of the 3596 participants, we first excluded participants with a diagnosed non-affective psychosis ($n = 74$). Then, we excluded all of the participants who had not been genotyped or did not have data on personality traits in any measurement year ($n = 1648$). Thus, a total of 1874 participants from the original sample were included in the analyses of the present study. In the statistical models, we also added covariates in a stepwise way, resulting in a sample size of 1328 participants in the fully-adjusted model. Taken together, our final sample size varied between 1328 and 1874 participants.

2.2. Measures

2.2.1. Polygenic risk scores for schizophrenia and major depression

Polygenic risk score for schizophrenia was calculated on the basis of the summary statistics from the latest genome wide association study of Schizophrenia Working Group of the Psychiatric Genomics Consortium (Trubetskoy et al., 2022). PRSscz was calculated using novel PRS-CS method. That is, all SNPs from GWAS summary statistics were considered when calculating the PRSSCZ. Specifically, clumping of SNPs in high LD was substituted by full LD modelling using HapMap 3 as external reference panel. A *p*-value threshold was substituted by using a Bayesian regression framework which includes all SNPs and applies continuous shrinkage priors to effect sizes. This shrinks SNPs with smaller effects sizes toward zero in the PRS_{SCZ} calculation. PRS-CS is proven to outperform conventional SNP clumping and *p*-value threshold selection in the prediction accuracy of complex traits, where the

mathematical basis of PRS-CS algorithm is thoroughly described, and performance tested with simulated and real-word data from the UK Biobank and Partners Healthcare Biobank (Ge et al., 2019). The latest available schizophrenia GWAS results (Trubetskoy et al., 2022) were used as SNP summary statistics and HapMap 3 EUR (The International HapMap 3 Consortium, 2010) as an external LD reference.

Polygenic risk score for major depression was calculated on the basis of study done by the Psychiatric Genomics Consortium (Howard et al., 2019). The details and calculation method of the risk score can be found in Supplementary Methods. PRS for major depression was used in our sensitivity analyses to investigate whether possible associations with personality traits are specific to PRS for schizophrenia or evident also for polygenic risk scores for other mental disorders such as major depression.

2.2.2. Personality traits

Personality traits were assessed in 2007 and 2012 using a Finnish translation of the NEO-FFI scale (Costa, 1989), which is a modified and shortened version of the NEO Personality Inventory. The inventory consists of 60 questions with 12 self-rated statements for each of the five traits. The scale measures Openness (e.g., "I am very curious intellectually"), Conscientiousness (e.g., "I strive for perfection in everything I do"), Extraversion (e.g., "I want to be surrounded by people"), Agreeableness (e.g., "I try to be polite to everyone I meet"), and Neuroticism (e.g., "I often feel tense and nervous"). The original NEO-PI includes six facets for each trait: for example, Neuroticism includes facets for Anxiety, Angry Hostility, Depression, Self-Consciousness, Impulsiveness, and Vulnerability to Stress. The NEO-FFI measures each facet with two items. We calculated a mean score between the measurement years for all the participants who had responded to at least 50 % of the items in at least one measurement year. In this sample, the NEO-FFI is shown to have high internal reliability (Cronbach's alpha = 0.89–0.91 for the subscales) (Lavonius et al., 2024). Regarding predictive validity, the NEO-FFI traits have been associated with health indicators such as sleep quality (Hintsanen et al., 2014) and job strain (Törnroos et al., 2013).

2.2.3. Psychiatric diagnoses

In the analyses, we excluded the participants diagnosed with a non-affective psychosis. Psychiatric diagnoses over participants' lifespan were collected in 2017 from the Finnish National Hospital Discharge Register, which covers all general and mental hospitals in Finland. In the register, the diagnoses were coded according to the diagnostic system in use at the time of diagnosis (ICD-8, ICD-9, or ICD-10). Then, the diagnoses were recoded to DSM-IV diagnoses and then pooled into categories, with one category being non-affective psychoses. The category of non-affective psychoses included the DSM codes of 295, 297, and 298, including to schizophrenia, schizophreniform disorder, schizoaffective disorder, delusional disorder, brief psychotic disorder, shared psychotic disorder, and psychotic disorder not otherwise specified). The procedure has been described with closer detail in a previous study (Sormunen et al., 2017). The register is shown to cover 93 % of schizophrenia-spectrum psychoses and 97 % of psychotic disorders (Sund, 2012) and, due to its high coverage, it has been used for research purposes also previously (Suvisaari et al., 1999).

In the sample of this study, a total of 74 participants had been diagnosed with a non-affective psychosis, resulting in a prevalence of 2.1 % that is close to the estimates given in previous prevalence studies (Kendler et al., 1996; Kessler et al., 2005). At the time of diagnosis collection, participants were between 40 and 55 years old and, thus, surpassed the typical age of onset of schizophrenia (Gureje, 1991; Häfner et al., 1993; Li et al., 2016).

2.2.4. Covariates

While age and sex can be regarded as basic covariates, we decided to control also for quality of early family environment, because PRS_{SCZ} is found to correlate with adversities in family enviornment (Newbury et al., 2022). Additionally, education was controlled for because high PRS_{SCZ} correlates with lower educational achievements (Sørensen et al., 2018) and education and Big Five personality traits are found to be genetically interconnected (Mõttus et al., 2017) and, thus, educational level might act as a confounder. The covariates were added in three blocks to investigate the stability of associations between PRS_{SCZ} and personality traits when controlling/not controlling for these psychosocial factors.

Quality of early family environment was assessed with parent-filled questionnaires in 1980. When necessary, we imputed missing values from the closest possible follow-up point (in 1983). We calculated a total of three cumulative risk scores indicating adversities in early family environment. *The cumulative score of stressful life events* included the following factors: changes of residence, changes of school, parental divorce (parents living together or separated), mother's or father's death, mother's or father's hospitalization within the past 12 months, and child's hospitalization due to sickness or accident. *The cumulative score of adverse socioeconomic circumstances* included parents' low occupational status, low educational level, low family income, an unstable employment situation, and an overcrowded apartment. *The cumulative score of unfavorable emotional family atmosphere* included an emotional distance between the child and parent, parental intolerance toward the child, strict discipline toward the child, parental life dissatisfaction, and mother's or father's frequent alcohol intoxication. The cumulative scores have been used previously and have been described previously (Saarinen et al., 2022).

Adulthood educational level was self-reported in 2011 and composed of three levels (1 = comprehensive school, 2 = high school or occupational school, 3 = academic level). Educational level was treated as continuous in the analyses.

2.3. Statistical analyses

In the analyses, we excluded the participants with a history of non-affective psychosis, because we were interested in the participants who have not developed a psychosis. Then, we used linear mixed models with full-information maximum likelihood estimation (MLE) to predict the trajectories of the personality traits with polygenic risk score for schizophrenia. Statistical assumptions for linear mixed models were checked by examining the normality of the residuals and homoscedasticity and were found to be approximately met. In the previous papers, missing values in the YFS data are found to be missing at random (see e.g. Pulkki-Råback et al., 2015, i.e., not including any systematic bias and, thus, full information maximum likelihood can be used to obtain unbiased estimates (Enders, 2010). Each personality trait was set as a dependent variable separately. The method of full-information MLE includes all the cases that have data available in at least one measurement year (i.e., 2007 or 2012). Linear mixed models estimate fixed and random effects. Briefly, fixed effects can be interpreted like traditional regression coefficients, whereas random effects focus on between-individual variance (individual differences) in the fixed intercept and slopes (Bolker et al., 2009). We estimated a fixed effect for the polygenic risk score for schizophrenia and for all of the covariates. We also examined possible curvilinear relationships between the polygenic risk score for schizophrenia and personality traits and, for this purpose, tested the statistical significance of the quadratic effect of the polygenic risk score for schizophrenia (PRS x PRS). Besides of the fixed effects, we estimated a random effect for the intercept (i.e., individual-level variance in the intercept). We did not include PRS_{SCZ} in the random effects because we were not primarily interested in the between-individual variance in its effect on Five-Factor traits. Instead, we were interested in its average effect (i.e., fixed effect) on Five-Factor traits in our population-based sample. Regarding covariates, we had three models with step-wisely added covariates. Models 1 were controlled for age and sex. Models 2 were additionally controlled for the three cumulative risk scores of early family environment. Models 3 were additionally

controlled for adulthood educational level.

As a sensitivity analysis, we reran the main analyses after excluding influential cases (+3 standard deviations in the PRSscz). As a specifity analysis, we were interested in whether possible associations with personality traits are specific to polygenic risk score for schizophrenia or whether they are also evident for polygenic risk scores for other mental disorders such as major depression. Therefore, we reran the main analyses so that the polygenic risk for major depression was included in the model.

Finally, we conducted attrition analyses to compare the study variables between included (n = 1874) and lost-to-follow-up (n = 1722) participants. The attrition analyses included Welch Two Sample t-tests, Wilcoxon rank sum tests, and Pearson's chi-square tests. We also calculated Cohen's d, Cramér's V, and rank-biserial correlation to estimate the effect sizes of the attrition.

When we examined the interaction between age and PRS we found that there were no significant results. The interaction between sex and PRS was found to be non-significant so we ran the main analyses for both sexes simultaneously.

The data analysis was conducted using SPSS version 28, and we visualized the results using STATA (SPSS, 2021; StataCorp, 2023).

3. Results

The means, standard deviations, frequencies, and measurement ranges of the study variables are presented in the Table 1.

3.1. Main analyses: PRS for schizophrenia predicting personality traits in participants with no history of non-affective psychosis

First, we examined possible curvilinear relationships between the PRS for schizophrenia and the personality traits (i.e., we included a quadratic effect of the PRS for schizophrenia as a predictor). We found a statistically significant quadratic effect of the PRS for schizophrenia when predicting Extraversion (B = −0.018; −0.020, 95 % CI = −0.033; −0.002, p = 0.024–0.030 in Models 1–3) but not when predicting any other personality trait. Thus, we dropped the quadratic effect of the PRS for schizophrenia from the models when predicting Openness, Neuroticism, Agreeableness, or Conscientiousness. The prediction of Extraversion is visualized in Fig. 1. Curvilinear predictions of all of the traits can be found in Supplementary Tables 1–5.

The results of the final analyses are presented in Table 2. The PRS for schizophrenia had a positive linear effect on Openness in all the models: in Model 1 (adjusted for age and sex, B = 0.029, 95 % CI = 0.006; 0.052, p = 0.014), in Model 2 (additionally adjusted for the cumulative risk score of early family environment, B = 0.030, 95 % CI = 0.007; 0.053, p = 0.011), and in Model 3 (additionally adjusted for adulthood education, B = 0.035, 95 % CI = 0.008; 0.062, p = 0.011). Additionally, the PRS for schizophrenia had a significant quadratic effect on Extraversion in Model 1 (B = −0.018, 95 % CI = −0.033; −0.002, p = 0.024), Model 2 (B = −0.018, 95 % CI = −0.034; −0.002, p = 0.024), and Model 3 (B = −0.020, 95 % CI = −0.038; −0.002, p = 0.030), while its linear effect was not significant (p = 0.154–718). In any of the models, the PRS for schizophrenia was not meaningfully associated with Neuroticism (p = 0.226–0.659 in Models 1–3), Conscientiousness (p = 0.065–0.281 in Models 1–3), or Agreeableness (p = 0.605–0.811 in Models 1–3). The results are illustrated in Fig. 1. More detailed results including estimates of the covariates can be found in Supplementary Tables 1–5.

3.2. Additional analyses

After finding the association of PRSscz to Openness and Extraversion, we ran additional analyses to examine the possible associations to the subscales of these traits. We calculated the subscales on the basis of a previous factor analytical study on NEO-FFI (Saucier, 1998). Regarding Openness, we found that PRSscz is significantly associated with Intellectual Interests in model 1 (B = 0.083, 95 % CI = 0.046; 0.119, p < 0.001), model 2 (B = 0.084, 95 % CI = 0.047; 0.121, p < 0.001), and model 3 (B = 0.098, 95 % CI = 0.056; 0.140, p < 0.001), but not with Aesthetic Interests or Unconventionality (p = 0.162–0.230; p = 0.540–0.846, respectively). Regarding Extraversion, PRSscz was significantly associated with Positive Affect in model 1 (B = −0.024, 95 % CI = −0.044; −0.005, p = 0.013), model 2 (B = −0.025, 95 % CI = −0.044; −0.005, p = 0.013), and model 3 (B = −0.032, 95 % CI = −0.054; −0.009, p = 0.005), but not with Activity or Sociability (p = 0.196–0.429; p = 0.125–0.144, respectively).

As a sensitivity analysis, we reran the main analyses after removing influential cases (+3 standard deviations in the PRSscz). The results of higher PRSscz predicting higher Openness held (B = 0.027, 95 % CI = 0.003; 0.051, p = 0.026). Next, as specificity analyses, we investigated whether possible associations with personality traits are specific to PRS for schizophrenia or whether they are also evident for polygenic risk scores for other mental disorders, such as major depression. Thus, we reran the main analyses with the PRS for major depression as a

Table 1
Descriptive statistics of the study variables in the sample. Note: This table includes all the participants who were included in at least one statistical analysis (n = 1874).

	Mean (*SD*)	Frequency (%)	Measurement range
Age in years (2007)	37.70 (5.05)		30–45
Sex (Male)		794 (42.4)	
Polygenic risk score for schizophrenia	−0.02 (1.00)		−4.72–2.94
Polygenic risk score for major depression	0.00 (0.001)		−0.003–0.002
Openness[a]			
2007	3.18 (0.53)		1–5
2012	3.11 (0.54)		1–5
Conscientiousness[a]			
2007	3.70 (0.56)		1–5
2012	3.73 (0.53)		1–5
Extraversion[a]			
2007	3.40 (0.55)		1–5
2012	3.39 (0.57)		1–5
Agreeableness[a]			
2007	3.69 (0.49)		1–5
2012	3.77 (0.49)		1–5
Neuroticism[a]			
2007	2.37 (0.66)		1–5
2012	2.50 (0.48)		1–5
Cumulative risk scores of early family environment (1980/1983)			
Stressful life events	−0.02 (0.40)		−0.50–2.24
Adverse socioeconomic circumstances	−0.02 (0.65)		−1.35–2.93
Unfavorable emotional family atmosphere	−0.03 (0.53)		−2.29–2.39
Educational level (2011)			
Comprehensive school		126 (9.3)	
Occupational school or high school		710 (52.4)	
Academic level		518 (38.3)	

[a] In the analyses, we used mean scores of the personality traits between the measurement years.

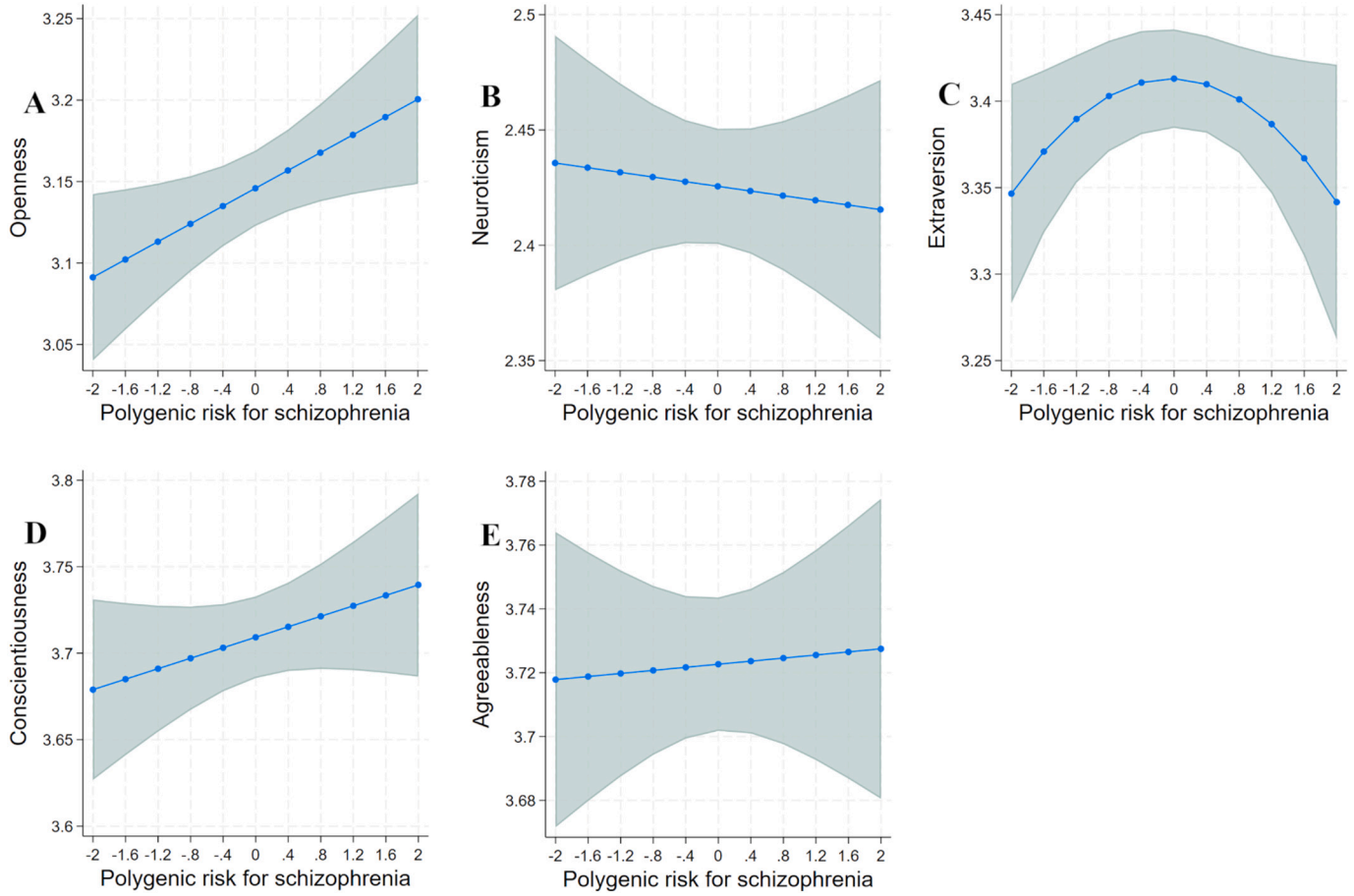

Fig. 1. Model-predicted values of (A) Openness (a significant linear effect), (B) Neuroticism, (C) Extraversion (a significant quadratic effect), (D) Conscientiousness, and (E) Agreeableness with 95 % confidence intervals (y-axis) at different values of polygenic risk score for schizophrenia (x-axis; scaled with the mean of 0 and SD of 1). Note: Adjusted for age and sex.

Table 2
Results of linear mixed models when predicting the Big Five personality traits with the polygenic risk for schizophrenia (PRS). Coefficients (B) with 95 % confidence intervals (CI) and standard errors (SE).

	Models 1 (n = 1872–1874)			Models 2 (n = 1803–1805)			Models 3 (n = 1328)		
	B (95 % CI)	*SE*	*p*	B (95 % CI)	*SE*	*p*	B (95 % CI)	*SE*	*p*
Openness									
PRS	**0.029 (0.006;0.052)**	**0.012**	**0.014**	**0.030 (0.007;0.053)**	**0.012**	**0.011**	**0.035 (0.008;0.062)**	**0.014**	**0.011**
Conscientiousness									
PRS	0.014 (−0.009;0.038)	0.012	0.231	0.013 (−0.011;0.037)	0.012	0.281	0.026 (−0.002;0.055)	0.014	0.065
Extraversion									
PRS	0.004 (−0.019;0.028)	0.012	0.718	0.008 (−0.016;0.032)	0.012	0.535	0.020 (−0.008;0.048)	0.014	0.154
PRS x PRS	**−0.018 (−0.033;-0.002)**	**0.008**	**0.024**	**−0.018 (−0.034;-0.002)**	**0.008**	**0.024**	**−0.020 (−0.038;-0.002)**	**0.009**	**0.030**
Agreeableness									
PRS	0.003 (−0.018;0.023)	0.011	0.811	0.004 (−0.017;0.025)	0.011	0.720	0.006 (−0.018;0.031)	0.012	0.605
Neuroticism									
PRS	−0.005 (−0.028;0.018)	0.012	0.659	−0.005 (−0.029;0.018)	0.012	0.653	−0.017 (−0.044;0.010)	0.014	0.226

Model 1 was controlled for age and sex.
Model 2 was additionally controlled for the cumulative risk score of early family environment.
Model 3 was additionally controlled for adulthood education.
Note: Fixed effects of the covariates as well as the random effects of the intercept were excluded from the table for clarity.
Note: Statistically significant ($p < 0.05$) models bolded.

covariate. The results mainly held, with the PRS for schizophrenia predicting higher Openness (B = 0.027, 95 % CI = 0.004; 0.050, $p = 0.022$) but not the other personality traits. The PRS for major depression did not predict any of the personality traits in any model (p = 0.078–0.594). More detailed results can be found in Supplementary Table 6.

3.3. Attrition analyses

Finally, we examined possible attrition bias between included and lost-to-follow-up participants. There was no significant attrition bias in the PRS for schizophrenia or PRS for major depression ($p = 0.095$ and $p = 0.828$, respectively). There were no significant differences between

included and lost-to-follow-up participants in Openness, Conscientiousness or Agreeableness ($p = 0.527$, $p = 0.188$, $p = 0.092$, respectively), but we found an attrition bias in Extraversion (3.40 vs 3.32, d = −0.152, $p = 0.006$) and Neuroticism (2.44 vs 2.52, d = 0.148, $p = 0.031$). Women were more likely to participate than men (57.6 % vs 43.7 %, v = 0.139, $p < 0.001$), and the included participants were slightly older than the lost-to-follow-up (37.70 vs 37.16, $r = -0.061$ $p = 0.001$). Included participants were more likely to have an academic-level education (38.3 % vs 20.2 %, v = 0.306, $p < 0.001$) than the lost-to-follow-up. Regarding early family environment, the included participants had slightly more favorable early family environment than the lost-to-follow-up (−0.034 vs 0.048, $r = -0.003$, p < 0.001 for emotional family atmosphere; −0.016 vs 0.021, $r = 0.043$, $p = 0.007$ for stressful life events, and − 0.020 vs 0.034, $r = 0.032$, $p = 0.020$ for socioeconomic adversities).

4. Discussion

The present study demonstrated that, in those who had not developed a non-affective psychosis, high PRS for schizophrenia predicted higher Openness in a linear manner. Additionally, PRS for schizophrenia had a curvilinear effect on Extraversion, indicating that low and high, but not average, levels of PRS for schizophrenia were related to lower Extraversion. In additional analyses we found that the PRS_{SCZ} was more specifically associated with the subfacets of Intellectual Interests from Openness, and Positive Affect from Extraversion. The PRS for schizophrenia was not meaningfully associated with Neuroticism, Conscientiousness, or Agreeableness. The PRS for major depression, in turn, did not meaningfully associate with any of the personality traits, indicating that the associations are not evident for polygenic risk scores for any mental disorder. In summary, individuals with high PRS may develop slightly different personality traits if they do not develop a non-affective psychosis.

Our results differ from the null findings between PRS_{SCZ} and Big Five personality traits reported in a UK sample of 16-year-old adolescents (Krapohl et al., 2015). We believe this discrepancy may be due to the age difference between the samples, as evidence suggests that many Big Five personality traits exhibit temporary dips during adolescence (around ages 16–17). Additionally, the lack of consideration for non-linear associations in their study may have contributed to the differing results.

Our results on PRS for schizophrenia and higher Openness have interesting parallels to previous studies. Openness to experience has been consistently shown to associate with creative achievements in arts and sciences and everyday creative activities (Jauk et al., 2014; Kaufman, 2013; Kaufman et al., 2016). Creativity, in turn, is linked to tendencies toward unusual experiences, impulsive or eccentric behavior (Batey and Furnham, 2008), and magical thinking (Gianotti et al., 2001; Mohr et al., 2001). Additionally, Openness can be regarded as a dimensional susceptibility factor for psychosis: it is linked to the psychoticism dimension of the Alternative Model of Personality Disorder and thought disorder dimension of the Hierarchical Taxonomy of Psychopathology (Kotov et al., 2021). Therefore, our results align with previous studies reporting associations of PRS for schizophrenia with creativity (Power et al., 2015) and magical thinking (Saarinen et al., 2022) and, in a recent study, positive schizotypy in men (Mas-Bermejo et al., 2025).

This study found a curvilinear association between PRS_{SCZ} and Extraversion. More specifically the PRS_{SCZ} was associated with the subscale of Positive Affect. It is likely, that the association with Positive Affect is capturing the affective component of the transdiagnostic psychosis risk (Reininghaus et al., 2016). Furthermore, the curvilinear nature of the finding (where both higher and lower PRS scores were associated with lower Extraversion) suggests, that the PRS for schizophrenia should not be viewed solely as a linearly growing risk factor, but also curvilinear associations should be considered. This raises an intriguing question of whether a certain degree of PRS for schizophrenia might actually be beneficial, or whether having extremely low PRS is optimal either. A previous study also reported some signs, though not strong, of possible nonlinear associations between PRS for schizophrenia and psychiatric symptoms in adolescence (Jones et al., 2016). Additionally, our findings on Extraversion suggest that there may be a health-promoting or beneficial developmental synchronies between polygenic liabilities and personality development. In individuals with high PRS for schizophrenia, low Extraversion is shown to predict decelerated epigenetic ageing, possibly due to not ending up in social situations that may be perceived as overwhelming or distressing (Saarinen et al., 2024).

PRS for schizophrenia was not related to higher Neuroticism, which was contrary to our expectations. Previously, PRS for schizophrenia has explained liability to disorders characterized by negative affect, such as generalised anxiety disorder and panic disorder (Richards et al., 2019), major depressive disorder (Ward et al., 2017), and also borderline personality disorder (Witt et al., 2017). Although not significant, we obtained a trend toward higher PRS for schizophrenia and slightly *lower* Neuroticism. Conceptually, Neuroticism refers to normal-range variance in personality. Thus, our results suggest that PRS for schizophrenia may be a better predictor of clinical conditions than of normal-range variation in negative affect. Further, a previous study found only two genetic loci shared between schizophrenia and Neuroticism (Smeland et al., 2017), indicating a relatively weak genetic intertwining.

Regarding limitations, there was some participant loss-to-follow-up in our prospective dataset when coming from the baseline assessment (in 1980) to the later follow-ups, with a final sample size of 1874 participants. Our attrition analyses indicated that there was no attrition bias in PRS for schizophrenia, PRS major depression, or most personality traits, i.e., Openness, Conscientiousness, or Agreeableness. Included participants had, however, slightly higher scores on Extraversion and lower scores in Neuroticism.

In conclusion, first, individuals with high PRS for schizophrenia, who have not developed non-affective psychosis, may still develop mildly different personality traits, specifically higher Openness and lower Extraversion. Second, some of these personality differences (that may be negatively valued in societies) may actually enhance their adaptation or promote their health: for instance, lower Extraversion is shown to protect them against accelerated epigenetic ageing (Saarinen et al., 2024).

CRediT authorship contribution statement

Veikka Lavonius: Writing – original draft, Visualization, Formal analysis, Conceptualization. **Liisa Keltikangas-Järvinen:** Writing – review & editing, Supervision, Resources, Methodology, Investigation, Funding acquisition. **Leo-Pekka Lyytikäinen:** Writing – review & editing, Methodology, Formal analysis. **Binisha Hamal Mishra:** Writing – review & editing, Methodology, Formal analysis. **Elina Sormunen:** Writing – review & editing, Methodology, Formal analysis, Data curation. **Mika Kähönen:** Writing – review & editing, Resources, Methodology, Funding acquisition. **Olli Raitakari:** Writing – review & editing, Resources, Methodology, Funding acquisition. **Jarmo Hietala:** Writing – review & editing, Resources, Methodology, Funding acquisition. **Terho Lehtimäki:** Writing – review & editing, Resources, Methodology. **Aino Saarinen:** Writing – review & editing, Supervision, Project administration, Conceptualization.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.schres.2025.05.017.

Data availability

The Cardiovascular Risk in Young Finns (YFS) dataset comprises health-related participant data, and their use is therefore restricted under the regulations on professional secrecy (Act on the Openness of Government Activities, 612/1999) and on sensitive personal data (Personal Data Act, 523/1999, implementing the EU data protection directive 95/46/EC). Due to these legal restrictions, the data from this study cannot be stored in public repositories or otherwise made publicly available. However, data access may be permitted on a case by case basis upon request. Data sharing outside the group is done in collaboration with YFS group and requires a data-sharing agreement. Investigators can submit an expression of interest to the chairman of the publication committee (Prof. Mika Kähönen, Tampere University, Finland, mika.kahonen@tuni.fi).

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