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Childhood Trauma Mediates the effects of Genetic Risk for Schizophrenia on Personality Traits

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Abstract

Schizophrenia is a severely debilitating psychiatric disorder that is typically presented with phases of relapse and remission. Despite being widely known, schizophrenia remains one of the top causes of disability in the world, causing severe personal and societal burden from long term disability. The symptoms and etiology of schizophrenia remain poorly understood, but recent developments in our understanding of psychiatric genetic risk are beginning to contribute to our grasp of psychiatric conditions, including schizophrenia. One of these developments are Polygenic Risk Scores (PRS), which are a measure of an individual's inherited liability to developing a trait, disease or disorder. Previous studies have shown that Schizophrenia Polygenic Risk Scores (SZ-PRS) and childhood trauma (CT) have strong associations with the Five-Factor Model (FFM) of Personality. This model, better known as the Big Five, divides personality into five traits: openness, conscientiousness, extraversion, agreeableness, and neuroticism. This thesis aims to examine the relationship between SZ-PRS and personality traits in a non-diagnosed population, subsequently looking into the possible gene-environment correlation between SZ-PRS and CT and examining the mediating role of CT in the relationship between SZ-PRS and personality traits. The analyses were performed using participants from the Utrecht Cannabis Cohort (N = 910). SZ-PRS were computed from the most recent Genome Wide Association Studies. The relationships between SZ-PRS, the FFM of personality and CT were first examined using linear regressions. Subsequently, mediation analyses of CT were performed to link the pathway of SZ-PRS to the FFM of personality. All analyses were corrected for age and sex. Our results are in line with previous research findings indicating that openness, conscientiousness, agreeableness and neuroticism are associated with SZ-PRS (B = .083, p = .020; B = -.112, p = .007; B = -.070, p = .039; B = .361, p = .017, respectively). No significant effect for extraversion was reported (B = -.073, p = .079). Furthermore, SZ-PRS was significantly associated with CT (B = .183, p = <.001), and CT was significantly associated with conscientiousness, extraversion, agreeableness and neuroticism (B = -.168, p = <.001; B = -.192, p = <.001; B = -.226, p = <.001; B = 1.215, p = <.001, respectively). Openness was not significantly affected by CT, thereby eliminating the possibility of a significant mediation effect. (B = .026, p = .253). The mediation analyses yielded results that indicate that CT fully mediated the relationship between SZ-PRS and agreeableness, extraversion and neuroticism and partially mediated the relationship between SZ-PRS and conscientiousness. Overall, age and sex displayed numerous group level differences across almost all analyses. Additional research is needed to support the current findings, but our results indicate that a genetic predisposition for developing schizophrenia influences the development of personality traits through the mechanisms of CT even before a clinical diagnosis.

Keywords*: Polygenic Risk Scores* | *Schizophrenia* | *The Big Five Personality Traits* | *Five Factor Model* | *Openness* | *Conscientiousness* | *Extraversion* | *Agreeableness* | *Neuroticism* | *Childhood Trauma* | *GWAS*

Schizophrenia is a severely debilitating psychiatric disorder that is typically presented with phases of relapse and remission. Schizophrenia is therefore often regarded as a chronic condition (Ermel et al., 2019; Kessler et al., 2012). The lifetime prevalence of schizophrenia (0,47%) is relatively low compared to other mental illnesses (Perälä et al., 2007; Tandon et al., 2008): e.g. major depressive disorder (11.32%; Gutiérrez-Rojas, 2008) and post traumatic stress disorder (10.10%; Kessler et al., 2012). Despite this, schizophrenia remains one of the top causes of disability in the world, causing severe personal and societal burden from long term disability (Charlson et al., 2018; Murray & Lopez, 1996). Schizophrenia is characterized by positive symptoms that distort the perception of reality (e.g. hallucinations and delusions), negative symptoms that lessen regular behavior (e.g. amotivation and social withdrawal) and cognitive symptoms (e.g. deficits in the working memory, processing speed and executive functions) (Charlson et al., 2018; Murray & Lopez, 1996).

Although schizophrenia is a widely known psychiatric condition, its symptoms and etiology remain poorly understood (Charlson et al., 2018; Galderisi et al., 2018; Szeligowski et al., 2020). Recently there have been major developments in our understanding of psychiatric genetic risk, one of which being Polygenic Risk Scores (PRS) (Legge t al., 2021). PRS are a measure of an individual's inherited liability to developing a trait, disease or disorder, and are beginning to contribute to our further understanding of psychiatric conditions, including schizophrenia (Ramos et al., 2019; Martin et al., 2018). Twin studies have established that schizophrenia has a strong genetic component and shared etiology with some personality traits, suggesting that genetic risk for schizophrenia might influence an individual's personality traits (Cardno & Gottesman., 2000; Mistry et al., 2018; Smeland et al., 2017; Sullivan et al., 2003). Furthermore, it has been well established that childhood trauma (CT) increases the risk and enhances the development of schizophrenia (Dvir et al., 2014; Loewy et al., 2019; Morgan & Fisher, 2007; Popovic et al., 2019; Schäfer & Fisher,

2020; Stanton et al., 2020) and even possible causal relationships have been proposed (Bolhuis et al., 2022; Polimanti et al., 2021). However, recent studies suggest that the effect of CT might also work vice versa. Recent insights by Marchi et al. (2022) have identified that increases in Polygenic Risk Scores for schizophrenia (SZ-PRS) are associated with greater exposure to CT, suggesting gene-environment correlations. Moreover, research indicates that CT could also have altering effects on an individual's personality traits (Paris, 1998; Li et al., 2014; Velikonja et al., 2019), suggesting that increased genetic risk for schizophrenia might alter personality traits through CT. Personality is considered to be a significant factor in the pathogenesis of schizophrenia due to it affecting a patients' symptoms, cognition, and social functioning (Compton et al., 2015; Gurrera et al., 2014). Furthermore, these personality alterations associated with CT resemble the personality traits often displayed in individuals with schizophrenia (Camisa et al., 2005; Gurrera et al., 2000; Ohi et al., 2012; Ohi et al., 2016). Overwhelming research, including meta analyses, suggests that patients with schizophrenia display a unique personality profile when compared to the general population (Camisa et al., 2005; Gurrera et al., 2000; Ohi et al., 2012; Ohi et al., 2016). It is therefore that this thesis aims to examine the relationship between SZ-PRS and personality traits in a non-diagnosed population, subsequently examining the mediating role of CT in the relationship between SZ-PRS and personality traits and looking into the possible gene-environment correlation between SZ-PRS and CT.

Twin- and other studies have established that schizophrenia has a strong genetic component (Cardno & Gottesman., 2000; Mistry et al., 2018; Sullivan et al., 2003). During the past decade, technological advances and falling costs have made Genome Wide Association Studies (GWAS) more accessible, allowing for an unbiased, data-driven approach to identify loci that are associated with schizophrenia (Cross-Disorder Group of the psychiatric Genomics Consortium, 2014). GWAS have identified multiple risk allele variants,

making schizophrenia, like many other common conditions, a polygenic disorder in most patients (Bassett & Chow, 2008; International Schizophrenia consortium et al., 2009; Misrty et al., 2018; Pantelis et al., 2014; Purcell et al., 2009; Schneider et al., 2014). Even though individual loci might only have small effects on the risk for developing schizophrenia, the information from even moderately associated alleles can be combined to form a single PRS. The PRS provides a genetic risk summary of the disorder based on the number of risk alleles an individual has, weighted by the odds ratio associated with each allele (Bassett & Chow, 2008; Schneider et al., 2014). The PRS can be used to examine how this genetic risk manifests across different populations and different stages of development (Wray et al., 2014). The genetic component of schizophrenia has heritability estimates ranging between 80-85% (Cardno & Gottesman., 2000; Mistry et al., 2018; Sullivan et al., 2003). Research by Smeland et al. (2017) discovered several loci that are shared between schizophrenia and openness, and schizophrenia and neuroticism, highlighting genetic loci involved in their common genetic etiology. These findings suggest that SZ-PRS might influence an individual's personality traits.

Thorough research has been conducted on the personality of individuals with schizophrenia using the Five-Factor Model (FFM), better known as the Big Five personality traits (Berenbaum & Fujita, 1994; Camisa et al., 2005; Gurrera et al., 2000; Kentros et al., 1997). The five major personality traits of the FFM are *openness*: a cognitive disposition towards creativity; *conscientiousness*: a tendency towards orderliness, self-discipline and dutifulness; *extraversion*: a disposition towards social interaction and assertiveness; *agreeableness*: a tendency towards being altruistic, sympathetic and trusting; and *neuroticism*: a vulnerability to self consciousness and emotional instability (Adanty et al., 2022; Ohi et al., 2016). Mounting evidence shows that patients with schizophrenia display higher levels of neuroticism, and lower levels of openness, conscientiousness, extraversion

and agreeableness, suggesting a unique character and personality profile when compared to healthy subjects (Camisa et al., 2005; Gurrera et al., 2000; Ohi et al., 2012; Ohi et al., 2016).

This unique personality profile exposes individuals to a diverse range of adverse effects. First, research shows that personality traits have a consistent and cumulative effect on an individual's health and lifespan (Caspi et al., 2005). For instance, low agreeableness and high neuroticism have been shown to predict poor physical health and earlier mortality (Lahey., 2009; Miller et al., 1996). Additionally, neuroticism is inversely associated with overall quality of life and occupational success (Ozer & Benet-Martinez, 2006) and growing evidence associates neuroticism with physical health problems such as cardiovascular disease (Suls & Bunde, 2005), asthma (Huovinen et al., 2001), and irritable bowel syndrome (Spiller., 2007).

Second, research shows that personality traits influence the development of an individual's psychopathology, because it predicts the onset and course of a disorder (Gleeson et al., 2005; Lonnqvist et al., 2009; Van Os & Jones, 2001). There is strong evidence that neuroticism is associated with many Axis I and II mental disorders such as, but not limited to, obsessive-compulsive disorder, borderline personality disorder, and schizophrenia (Khan et al., 2005; Krueger et al., 2001; Watson et al., 1994). Moreover, research by Trull and Sherr (1994) has linked neuroticism and low extraversion to increased incidences of depression.

Third, personality traits influence substance use and antisocial behavior. High neuroticism, low conscientiousness, and low agreeableness are all robustly associated with the use and abuse of psychoactive substances such as alcohol, nicotine, and heroin (Kornør & Nordvik, 2007; Malouff et al., 2007; Walton & Roberts, 2004), potentially increasing further health deterioration and psychopathology (Mirin et al., 1991; Swensen., 2015). Thus, there is overall strong evidence from prospective studies that the unique personality profile seen in individuals with schizophrenia is related to adverse outcomes.

Although schizophrenia has a strong genetic component, even among identical twins pairwise concordance is only around 50%, highlighting the importance of gene-environment correlations to increase schizophrenia risk (Hilker et al., 2018; Kendler & Eaves, 1986; Plomin et al., 1977). Recent studies shed new insights on the possible gene-environment correlations of SZ-PRS and CT (Bolhuis et al., 2022; Marchi et al., 2022). It has been well established that childhood trauma (CT) increases the risk and enhances the development of schizophrenia (Dvir et al., 2014; Loewy et al., 2019; Morgan & Fisher, 2007; Popovic et al., 2019; Schäfer & Fisher, 2020; Stanton et al., 2020) and even possible causal relationships have been proposed (Bolhuis et al., 2022; Polimanti et al., 2021). However, recent studies suggest that the effect of CT might also work vice versa. A study by Marchi et al. (2022) further supports recent findings that suggest a gene-environment correlation between SZ-PRS and CT (Bolhuis et al., 2022). Bolhuis et al. (2022) suggests that higher SZ-PRS can predict worse mental health in children through an increased risk of experiencing CT. Additionally, research indicates that CT could also have altering effects on an individual's personality traits (Paris, 1998; Li et al., 2014; Velikonja et al., 2019). A recent study by Adanty et al. (2022) found associations between exposure to any form of childhood abuse and an increase in neuroticism. Their research also found that exposure to certain forms of CT (e.g. sexual abuse, emotional abuse, physical neglect) are associated with decreased openness, conscientiousness, extraversion, and agreeableness. These personality alterations resemble the typical personality profile displayed in individuals with schizophrenia (Camisa et al., 2005; Gurrera et al., 2000; Ohi et al., 2012; Ohi et al., 2016).

Studies have demonstrated that age and sex impose differences on the manifestations of personality traits as well (Kawamoto et al., 2015; Vecchione et al., 2012;). A large study (N = 19.022) by Lehmann et al. (2013) found significant age differences for the FFM personality traits and a study by Hori et al. (2009) has shown that sex differences have been

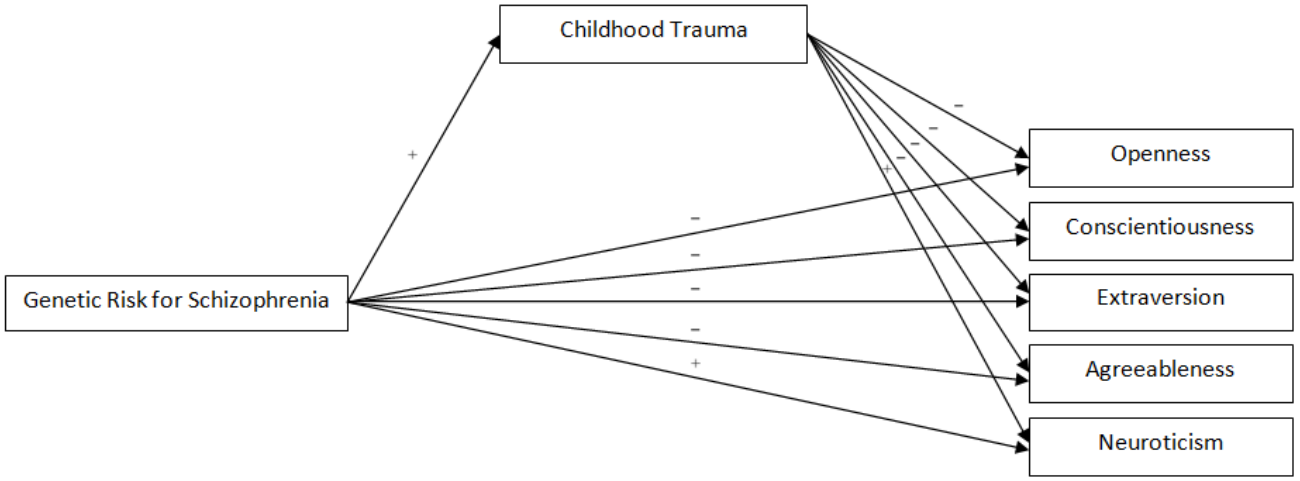
shown to affect age of onset, premorbid functioning symptomatology, and neuropsychological functioning in individuals with schizophrenia (Hori et al., 2008).

Considering the importance of the genetic component of schizophrenia and the typical personality profile displayed by individuals with schizophrenia, this thesis aims to investigate the relationship between SZ-PRS and the FFM personality traits in a non-diagnosed population. A non-diagnosed population was used due to the homogeneity of personality traits and SZ-PRS of individuals with diagnosed schizophrenia (Camisa et al., 2005; Gurrera et al., 2000; Jonas et al., 2019; Ohi et al., 2012; Ohi et al., 2016). The analyses were extended by looking into the possible gene-environment correlation between SZ-PRS and CT, and examining the mediating role of CT in the relationship between SZ-PRS and the FFM personality traits. All analyses will be corrected for age and sex due to the significant differences that have been found between the relationship of age and sex on personality traits.

This thesis hypothesizes that SZ-PRS is associated with differences in personality traits, namely higher neuroticism and lower openness, conscientiousness, extraversion, and agreeableness (H1). Secondly, whether SZ-PRS is associated with increased CT (H2). Finally, hypothesizing that higher levels of CT acts as a mediator that links higher levels of SZ-PRS to lower openness, conscientiousness, extraversion and agreeableness and higher neuroticism (H3) (see Figure 1). The results of this study could help unravel more understanding on how schizophrenia influences the development of personality traits and shapes psychological mental health, thereby possibly assisting in the development of targeted early detection and prevention for the non-diagnosed population that are at increased risk of developing schizophrenia.

Figure 1

Overview of the hypothesized relationships between the variables studied in this thesis



Note. The arrows indicate the direction of the relation, the '+' indicates a positive effect and the '-' indicates a negative effect. All hypothesized relationships are displayed into a single figure due to the limitations multiple figures would provide. It is notable that the analyses were not performed in a single model and this figure is merely a visualized representation of the hypotheses examined in this thesis.

Methods

Participants

The sample consists of N = 910 individuals aged between 16 to 28 years (M = 20.36, SD = 2.141) and includes 428 males (47.0%) and 482 females (53.0%). This sample is part of the Utrecht Cannabis Cohort (UCC) and was recruited using a website that was launched in 2006 (Schubart et al., 2011). A selected sampling strategy was implemented for the UCC which aimed to increase the detection power of the gene-environment interaction (Boks et al., 2007; Stringer et al., 2016). The study was approved by the University Medical Center Utrecht medical ethics committee, all participants have participated on a voluntary basis and

have provided written informed consent for their participation in the study (Marchi et al., 2022).

Measures

The self-report Childhood Trauma Questionnaire (CTQ) was utilized to assess a participant's exposure to CT (Bernstein et al., 1994). The CTQ measures five categories of self-reported childhood abuse: physical abuse, emotional abuse, sexual abuse, emotional neglect and physical neglect (Bernstein et al., 2007). Respondents rate their agreement to a total of 25 statements on a Likert scale ranging from 1 to 5 (1 = Never True, 2 = Rarely True, 3 = Sometimes True, 4 = Often True, 5 = Very Often True). For example, to measure the exposure to emotional neglect, the respondent had to rate their agreement with the statement "I felt like there was someone in my family who wanted me to be a success" (Bernstein et al., 1994). Every category of childhood abuse is represented by five statements in the CTQ, hence why the minimum score for each category of childhood abuse is 5 and the maximum score is 25. The CTQ is a validated questionnaire and has been widely used in both research and clinical settings with a Cronbach's Alpha level of .95 for the total scale (Bernstein et al., 1994; Macdonald et al., 2015; Ni et al., 2021). The continuous sum score of the CTQ was used as a measure of CT.

The NEO-Personality Inventory-Revised (NEO-PI-R) was used to assess a participant's personality traits (Mõttus et al., 2019). The NEO-PI-R is a standardized self-report questionnaire consisting of 240 items that provides a quantitative measurement of the respondents' five domains of personality, following the Five-Factor model (Mõttus et al., 2019). The Five-Factor model of personality traits consist of: *openness*, *conscientiousness*, *extraversion*, *agreeableness* and *neuroticism* (McCrae & John, 1992). Respondents rate their agreement to the 240 statements on a Likert scale ranging from 1 to 5 (1 = Strongly Disagree, 2 = Disagree, 3 = Neither Agree nor Disagree, 4 = Agree, 5 = Strongly Agree) (Mõttus et al.,

2019). For example, to measure extraversion, the respondent had to rate their agreement with the statement "I like having a lot of people around me". Every personality dimension is represented by 48 statements in the NEO-PI-R, hence why the minimum score for each personality dimension is 48 and the maximum score is 240 (Xie & Cobb, 2020). The NEO-PI-R is a validated questionnaire which is widely used in research and clinical practice to assess personality. The Neo-PI-R has Cronbach's Alpha values ranging between .84 to .92 with a median of .88 (Mõttus et al., 2019; Rossier et al., 2004). The continuous sum score of each of the NEO-PI-R personality traits was used as a measure of personality.

Genetic Data - Polygenic Risk Scores Selection

The SZ-PRS has been calculated by Marchi et al. (2022) for every individual of the UCC who passed the genetic CQ, using PRsice2 (Choi & O'Reilly, 2019). Only autosomes were included in the data for the calculation of the SZ-PRS (Choi et al., 2020). The most recent GWAS data containing 40.675 cases and 64.643 controls was used to produce the SZ-PRS (Pardiñas et al., 2018). Marchi et al. (2022) calculated the SZ-PRS for each individual with the use of thirteen different *p*-value thresholds (*pt*). The *pt* consisted of: $5*10^{-8}$, $5*10^{-7}$, $5*10^{-6}$, $5*10^{-5}$, $5*10^{-4}$, $5*10^{-3}$, $5*10^{-2}$, 0.5, 0.4, 0.3, 0.2, 0.1, 1; of which one optimal threshold was selected. These *pt* are instated to help exclude alleles that have no significant influence on the risk of developing schizophrenia. To help identify which *pt* constitutes as the best predictor within the sample, Marchi et al. (2022) used a LASSO regression analysis correcting for age, sex and the first three principal components. Research has shown that this is the most effective way to select the right predictor from a set of variables (Ni et al., 2021). If multiple SZ-PRS-*pt* were identified by the LASSO analysis, a selection was made selecting the SZ-PRS-*pt* with the highest explained variance as depicted by the regression model (i.e., the R^2). Using a LASSO regression, Marchi et al. (2022) selected an optimal SZ-PRS-*pt* which yielded three out of thirteen SZ-PRS-*pt* as the best

predictors. Marchi et al. (2022) found that the highest explained variance was found with SZ-PRS pt 0.5 (R^2=0.014), which was selected as the best indicator of the genetic risk to schizophrenia in the subsequent analyses.

Data-analyse

To test for mediation Baron and Kenny (1986) propose a four step approach including several regression analyses, whereby the significance of the coefficients is evaluated at each step. Baron and Kenny (1986) advise that if one or more of these relationships is not significant further analyses should be halted, because mediation will not be possible or not very likely, although this is not always the case (Fairchild & Fritz, 2007). Hayes (2013) has shown that there does not need to be a significant direct effect in order to establish mediation, as significant indirect paths are deemed sufficient. Considering these insights, further analyses will not be halted if only the main effect is not significant, but only if any of the other effects do not show significance.

Following the combined approach of Baron and Kenny (1986) and Hayes (2013); first, linear regressions were used to examine the relationship between SZ-PRS and openness, conscientiousness, extraversion, agreeableness and neuroticism, adding age and sex as covariates. Second, a linear regression was used to examine the relationship between SZ-PRS and CT, adding age and sex as covariates. Third, a linear regression was used to examine the relationship between CT and openness, conscientiousness, extraversion, agreeableness and neuroticism, adding age and sex as covariates. Fourth, CT was added into the first model as a covariate alongside age and sex to test for the possibility of mediation. Lastly a mediation analysis was performed to assess the effect of SZ-PRS on openness, conscientiousness, extraversion, agreeableness and neuroticism directly and indirectly through CT; whilst also applying 5000 bootstraps with a 95% confidence interval (adding age and sex as covariates) to test for significance. The statistical analyses were performed using SPSS, using the SPSS

add-on PROCESS V3.5 for the mediation analysis. The sample size was calculated using the tool G*Power (Faul et al., 2019). This determined that a minimum of 395 participants were needed to provide sufficient power (1-β error prob = 0.80) to detect a small effect size (f 2 = 0.02) using linear regressions.

Data preparation and missing data

Participants who failed to provide at least one NEO personality-trait score were excluded (n = 353). Any participants who did not provide a total CTQ score were excluded (n = 1). A box plot was used to determine outliers for the variable age. Based on the boxplot n = 5 extreme outliers (≥ 3 x Interquartile Range) were excluded. No further missing data was present in the sample. Therefore no missing data strategy has been implemented.

Results

Checking descriptives and assumptions

Prior to the regression analyses, the variables were checked for linearity, normality independece, multicollinearity and heteroscedasticity. All VIF analysis showed values ≤ 1.02 (see Appendix A). Heteroscedasticity was checked using scatterplots. Normality was checked using pp plots, histograms and the Shapiro-Wilks test. SZ-PRS was the only variable that showed normality according to the Shapiro-Wilks test (see Appendix A). No further significant breaches of the assumptions were detected. The assumption checks were repeated with the dataset where no one was excluded based on age to test for significant differences in the results. Resulting in a breach of the assumption of homoscedasticity. Thus, the dataset excluding participants for age was used for further analyses.

Descriptive Statistics and Correlations for the Variables

The descriptive statistics and correlations for SZ-PRS, openness, conscientiousness, extraversion, agreeableness, neuroticism and CT (corrected for age and sex) can be found in

Table 1. Additional statistical information regarding these analyses can be found in Appendix A.

Table 1

Correlations and Descriptive Statistics for the Study Variables

Variable	*N*	*M*	*SD*	*1*	*2*
1. SZ-PRS [a]	910	-292.25	5.32	–	
2. Childhood Trauma [a b]	910	31.90	8.40	.183**	–
3. Openness [a b]	910	39.92	5.81	.083*	.026
4. Conscientiousness [a b]	910	41.50	6.88	-.112**	-.168**
5. Extraversion [a b]	910	41.79	6.64	-.073	-.192**
6. Agreeableness [a b]	910	43.72	5.68	-.070*	-.226**
7. Neuroticism [a b]	910	130.82	24.64	.361*	1.215**

[a] Linear Regression analysis with age and sex as covariates.

[b] *M* = the mean continuous sum scores of the respective questionnaire.

*$p < .05$. **$p < .01$.

Regression analyses (H1)

The first hypothesis stated that increased SZ-PRS is associated with differences in personality traits, namely higher neuroticism and lower openness, conscientiousness, extraversion and agreeableness. Table 1 shows that SZ-PRS has a significant positive correlation with openness and neuroticism (B = .083, p = .020; B = .361, p = .017, respectively), a significant negative correlation with conscientiousness and agreeableness (B = -.112, p = .007; B = -.070, p = .039, respectively) and no significant correlation with extraversion (B = -.073, p = .079). These findings confirm the hypothesis that SZ-PRS is correlated with higher neuroticism and lower conscientiousness and agreeableness. The results did not show a negative correlation of SZ-PRS on openness and no significant

correlation of SZ-PRS on extraversion, thereby rejecting their hypotheses. Age and sex are significant for all mentioned analyses with the only exception being that of age on neuroticism which was non-significant (B = .-.393, p = .296). This indicates that there are statistically significant differences in personality traits between the group levels of both age and sex.

Regression analysis (H2)

The second hypothesis stated that SZ-PRS is associated with increased CT. Table 1 shows that SZ-PRS has a significant positive correlation with CT (B = .183, p = <.001), confirming H2. Age and sex were both not significant (B =.228 , p = .078, B = -.962, p = .083), indicating no significant difference in group levels.

Testing the Possibility of Mediation

Openness did not show a significant correlation with CT and will therefore be excluded from further mediation analyses (B = .026, p = .253). To test for the possibility of mediation, the main effect model of SZ-PRS on the four remaining personality traits (conscientiousness, extraversion, agreeableness and neuroticism) was extended by adding CT as a covariate alongside age and sex. Table 2 shows that SZ-PRS has a significant positive correlation with conscientiousness (B = -.083, p = .046) and no significant correlation with extraversion, agreeableness and neuroticism. Thus indicating a possible mediating effect of CT on the relationship between SZ-PRS and extraversion, agreeableness and neuroticism, and the absence of a mediating effect for conscientiousness. Therefore, further analyses were performed to test for mediation. All covariates (CT, age and sex) were significant with the exceptions of age not being significant for extraversion and neuroticism (B = -.098, p = -.974; B = -.668, p = .052, respectively) and sex not being significant for extraversion (B = -.124, p = -.287). This indicates that there are statistically significant differences in

personality traits between the group levels of both age and sex, as well as that CT might be moderating the effect between SZ-PRS and personality traits.

Table 2

Mediation Analysis for CT between SZ-PRS and Personality Traits controlled for Age, Sex and CT

Variables	*B*	*t*	*p*	R-squared
Conscientiousness	-.083	-2.000	.046	.091
Extraversion	-.038	-.943	.346	.062
Agreeableness	-.029	-.903	.367	.202
Neuroticism	.141	1.018	.309	.201

Note. N = 910

Mediation Analysis Openness (H3)

The third hypothesis stated that CT acts as a mediator that links SZ-PRS to increased differences in personality traits. with higher levels of SZ-PRS being correlated with higher levels of CT and lower openness. No further analyses were performed for openness due to the absence of a significant association with CT, thereby eliminating the possibility of a significant mediation effect.

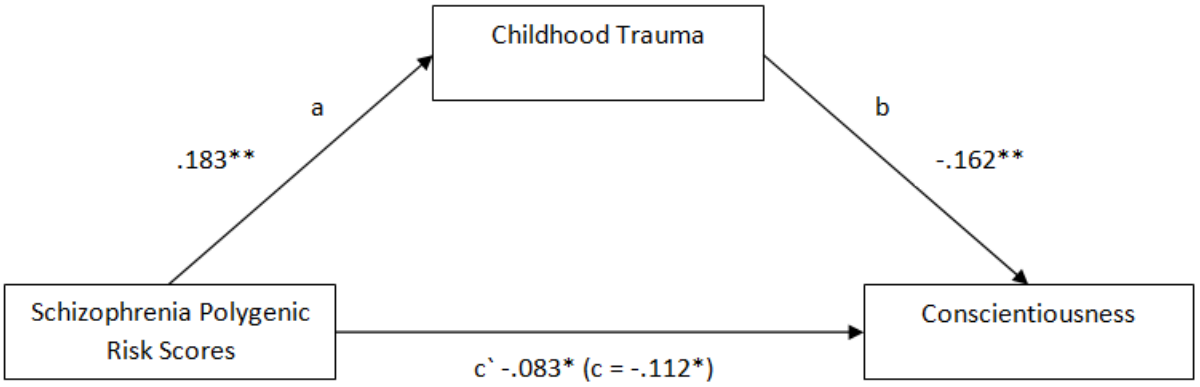
Mediation Analysis Conscientiousness (H3)

This study assessed the mediating role of CT on the relationship between SZ-PRS and conscientiousness, hypothesizing that higher levels of SZ-PRS are associated with higher levels of CT and lower conscientiousness (H3). The results revealed a significant negative indirect effect of SZ-PRS on conscientiousness through CT (F = 16.71, B = -.030, 95% CI [-.0510 – -.0122]), supporting H3. Furthermore, the direct effect of SZ-PRS on conscientiousness in the presence of CT (c`) was also found significant (F = 16.71, B = -.083, p = .046). Hence, indicating that CT partially mediates the relationship between SZ-PRS and conscientiousness (see Figure 2; full model R^2 = .052). Age and sex were both

non-significant in the relationship between SZ-PRS and CT (a) (B = .228, p = .078; B = -.962, p = .084, respectively). Thus, indicating that there are no statistically significant group level differences of both age and sex in the relationship between SZ-PRS and CT. This relationship is identical in every mediation analysis performed and will therefore not be mentioned in subsequent results. In the full model age and sex are both significant (B = .337, p = .001; B = -2.806, p = <.001, respectively). This indicates that there is a statistically significant group level difference of both age and sex in the full model relationship between SZ-PRS and conscientiousness mediated by CT.

Figure 2

Mediation Model for the Mediating role of CT on the relationship between SZ-PRS and Conscientiousness



Note. Total N = 910. Coefficients presented are unstandardized regression coefficients. c = total effect. *p < .05. **p < .001.

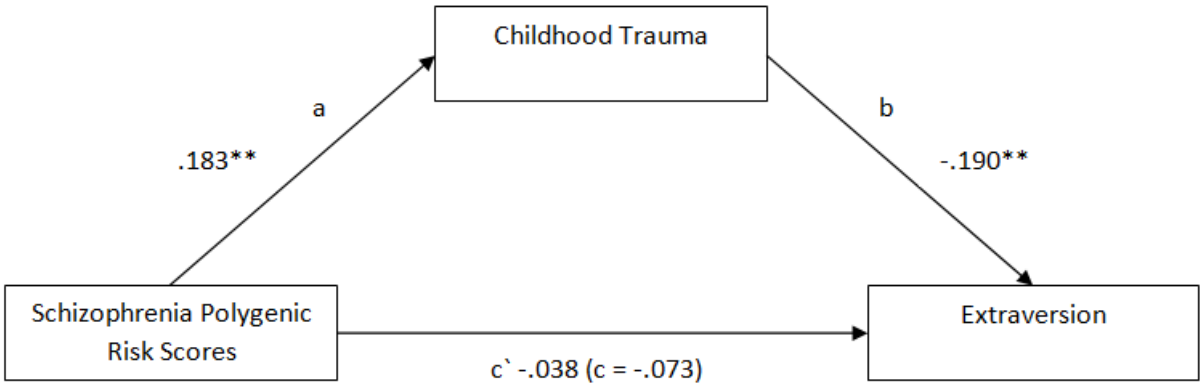
Mediation Analysis Extraversion (H3)

This study assessed the mediating role of CT on the relationship between SZ-PRS and extraversion hypothesizing that higher levels of SZ-PRS are associated with higher levels of CT and lower extraversion (H3). The results revealed a significant negative indirect effect of SZ-PRS on extraversion through CT (F = 1.65, B = -.035, 95% CI [-.0606 ; -.0145]), supporting H3. Furthermore, the direct effect of SZ-PRS on extraversion in the presence of

CT (c`) was found non-significant (F = 1.65, B = -.038, p = .346). Thus, indicating that CT fully mediates the relationship between SZ-PRS and extraversion (see Figure 3; full model R^2 = .005). In the full model age and sex are both non-significant (B = -.098, p = .331; B = -.124, p = .774, respectively). This indicates that there are no statistically significant group level differences of both age and sex in the full model relationship between SZ-PRS and extraversion mediated by CT.

Figure 3

Mediation Model for the Mediating role of CT on the relationship between SZ-PRS and Extraversion



Note. Total N = 910. Coefficients presented are unstandardized regression coefficients. c = total effect. *p < .05. **p < .001.

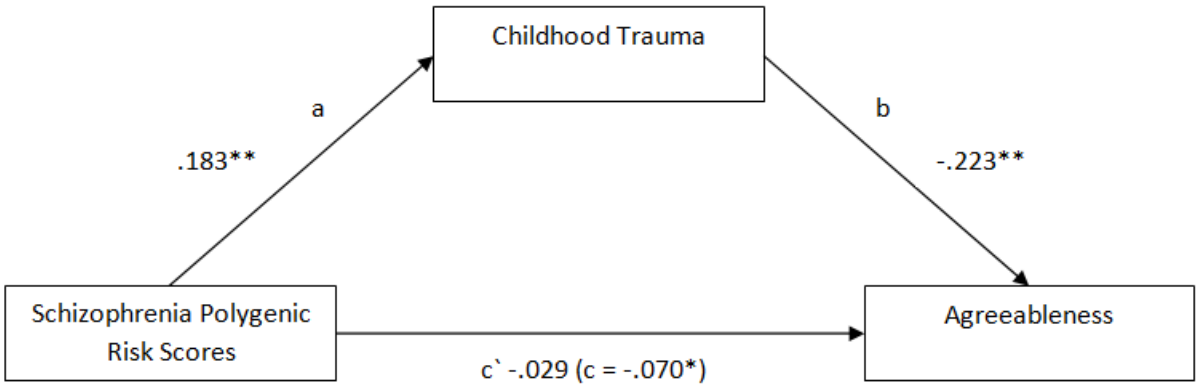
Mediation Analysis Agreeableness (H3)

This study assessed the mediating role of CT on the relationship between SZ-PRS and agreeableness hypothesizing that higher levels of SZ-PRS are associated with higher levels of CT and lower agreeableness (H3). The results revealed a significant negative indirect effect of SZ-PRS on agreeableness through CT (F = 31.48, B = -.040, 95% CI [-.0658 ; -.0194]), supporting H3. Furthermore, the direct effect of SZ-PRS on agreeableness in the presence of

CT (c`) was found non-significant (F = 31.48, B = -.029, p = .367). Thus, indicating that CT fully mediates the relationship between SZ-PRS and agreeableness (see Figure 4; full model R^2 = .094). In the full model age and sex are both significant (B = .318, p = <.001; B = -3.468, p = <.001, respectively). This indicates that there is a statistically significant group level difference of both age and sex in the full model relationship between SZ-PRS and agreeableness mediated by CT.

Figure 4

Mediation Model for the Mediating role of CT on the relationship between SZ-PRS and Agreeableness



Note. Total N = 910. Coefficients presented are unstandardized regression coefficients. c = total effect. *p < .05. **p < .001.

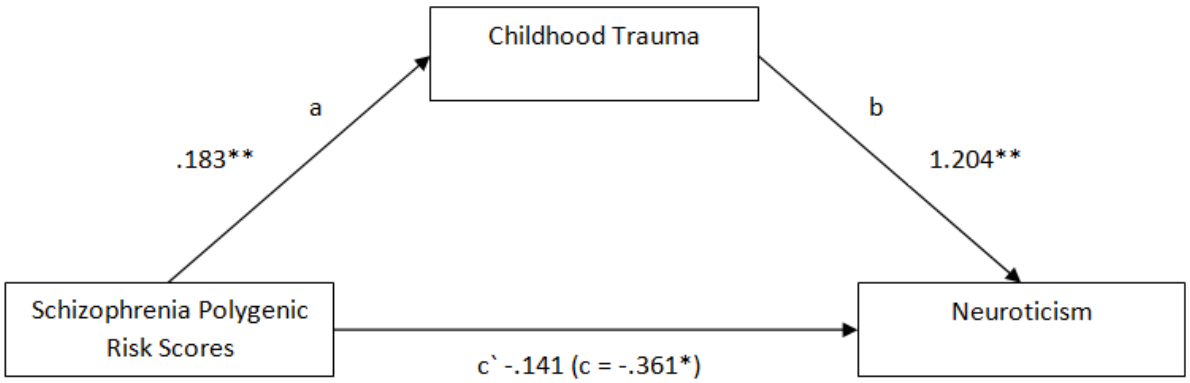
Mediation Analysis Neuroticism (H3)

This study assessed the mediating role of CT on the relationship between SZ-PRS and neuroticism hypothesizing that higher levels of SZ-PRS are associated with higher levels of CT and higher neuroticism (H3). The results revealed a significant positive indirect effect of SZ-PRS on neuroticism through CT (F = 11.24, B = .220, 95% CI [.1005 ; .3509]), supporting H3. Furthermore, the direct effect of SZ-PRS on neuroticism in the presence of CT (c`) was found non-significant (F = 11.24, B = .141, p = .309). Hence, indicating that CT fully mediates the relationship between SZ-PRS and neuroticism (see Figure 5; full model R^2

= .036). In the full model sex was significant (B = -7.235, p = <.001), but age was non-significant (B = -.668, p = .052). This indicates that there is a statistically significant group level difference for sex, but not for age in the full model relationship between SZ-PRS and neuroticism mediated by CT.

Figure 5

Mediation Model for the Mediating role of CT on the relationship between SZ-PRS and Neuroticism



Note. Total N = 910. Coefficients presented are unstandardized regression coefficients. c = total effect. *p < .05. **p < .001.

Additional statistical information regarding the direct, indirect and total effects of all mediation analyses can be found in appendix A. Additional statistical values for the covariates age and sex regarding all analyses performed in this thesis can also be found in appendix A.

Discussion

This thesis investigated the relationship between genetic risk for schizophrenia (SZ-PRS) and the Five-Factor Model (FFM) of personality traits: openness, conscientiousness, extraversion, agreeableness and neuroticism. The research was extended

to further investigate whether childhood trauma (CT) has a mediating role in this relationship whilst controlling for age and sex on all analyses. Results showed that higher SZ-PRS is positively associated with neuroticism and openness and negatively associated with conscientiousness and agreeableness. No effect for extraversion was reported. The mediation analyses yielded results that indicated that CT fully mediated the relationship between SZ-PRS and agreeableness, extraversion and neuroticism, and partially mediated the relationship between SZ-PRS and conscientiousness. No mediation was performed for openness due to the absence of a significant association with CT, thereby eliminating the possibility of a significant mediation effect. Overall, age and sex displayed numerous group level differences across almost all analyses with one major exception of finding no group level difference in the relationship between SZ-PRS anc CT.

Hypothesis 1: SZ-PRS and Personality Traits

Higher SZ-PRS were associated with higher neuroticism and openness and lower conscientiousness and agreeableness in this sample, whilst SZ-PRS was not associated with extraversion. Numerous studies support the results of this thesis by showing positive associations between SZ-PRS and neuroticism and negative associations between SZ-PRS, conscientiousness and agreeableness (Camisa et al., 2005; Duncan et al., 2018; Gale et al., 2016; Whalley et al., 2016). However, conflicting results were also reported. Multiple different studies found contradicting results to our current findings, with negative associations between SZ-PRS and extraversion and positive associations between SZ-PRS, openness and agreeableness (Berenbaum & Fujita, 1994; Duncan et al., 2018; Gale et al., 2016; Han et al., 2012; Lo et al., 2017; Whalley et al., 2016). Han et al. (2012) hypothesize that the increase in agreeableness might be a reaction to the impairment of other functions in individuals with high SZ-PRS. Duncan et al. (2018) and Power et al. (2015) suggest that the positive association between SZ-PRS and openness could be due to SZ-PRS being predictive

for artistic occupations in the general population and openness being the personality dimension that is the closest related to aesthetic design and art (Costa & McCree, 1992; George & Zhou, 2001; McCrae, 1987). When interpreting the results it is important to note that the study regarding agreeableness only had a small sample size consisting of 26 participants (Han et al., 2012).

Hypotheses 2 and 3: Mediation Analyses of CT

The results of this study showed that CT fully mediates the relationship between SZ-PRS and agreeableness, extraversion and neuroticism, and partially mediates the relationship between SZ-PRS and conscientiousness. A requirement for mediation is a significant relationship between the independent variable and the mediator (a path) and between the mediator and the dependent variable (b-path) (Baron & Kenny, 1986; Hayes, 2013). Our findings reported a positive result between SZ-PRS and CT. These results further strengthen recent findings, including a systematic review and meta-analysis, which all found positive associations between SZ-PRS and CT (a-path) (Bolhuis et al., 2022; Marchi et al., 2022; Woolway et al., 2022). Furthermore, our current findings for the relationship between CT and conscientiousness, extraversion, agreeableness and neuroticism (b-path) are supported by a recent study which found that exposure to certain forms of CT (e.g. sexual abuse, emotional abuse, physical neglect) were associated with increased neuroticism and decreased conscientiousness, extraversion and agreeableness (Adanty et al., 2022). Adanty et al. (2022) also found certain forms of CT to be negatively associated with openness, which this thesis was not able to replicate. However, results from a large sample study by Allen and Lauterbach (2007) found that individuals that have experienced CT displayed increased levels of openness. These results are conflicting with the findings of Adanty et al. (2022). This deviating result is further supported by research that found positive associations between openness and reports of greater stress endurance during childhood (Williams et al., 2009).

These divergent findings could explain why the current study was not able to replicate these earlier findings. To the best of our knowledge no prior research was conducted investigating the mediating role of CT in the relationship between SZ-PRS and personality traits.

Age and sex

The results of this thesis showed that the group level of both age and sex impacted the differences in personality traits as they influenced almost every analyses performed. The two exceptions being that (1) age was not shown to be associated with the relationship between SZ-PRS and neuroticism and (2) age and sex were not associated with the full mediation model of CT on the relationship between SZ-PRS and extraversion. Thus indicating that individual differences in age and sex influence the relationship between SZ-PRS and openness, conscientiousness, extraversion, agreeableness and neuroticism, and additionally influence the current mediation models of conscientiousness, agreeableness and neuroticism. These results align with multiple studies, including a large sample study (N = 19.022; Lehmann et al., 2013) that found that openness, conscientiousness, extraversion, agreeableness and neuroticism were all associated with age and sex (Kawamoto et al., 2015; Vecchione et al., 2012;). These results further support insights into the important role of age and sex as covariates.

Strengths

Despite some limitations, this study provides relevant insights to the scientific field. To the best of our knowledge this is the first study that investigated the relationship of SZ-PRS on personality traits and the mediating role of CT in this relationship. Other research has previously focussed on the relationship between SZ-PRS and psychotic symptoms and the mediating effect of CT (Marchi et al., 2022). Furthermore the current sample consists of N = 910 which is far more than the minimum requirement for the current study design (N = 395). Whilst a large sample size is good for the reliability, normal distribution and

generalizability of a sample, it runs the risk of finding guaranteed significant effects (Khalilzadeh & Tasci., 2017). It is for this reason that it is important to mention the practical significance in the form of effect-sizes (i.e. R^2). Furthermore, the questionnaires used in this study (CTQ and NEO-PI-R) are considered to be highly reliable and valid and are currently widely used in research and clinical practice (Macdonald et al., 2015; Mõttus et al., 2019; Ni et al., 2021;).

Limitations

Most variables did not indicate normal distributions according to the Shapiro-Wilks test. Although this test is regarded as one of the most sensitive normality tests (Ahad et al., 2011), research has shown that sample sizes greater than 85 were found to generate stable standard deviations and means regardless of the level of skewness (Piovesana & Senior, 2018). Additionally, the UCC consists of participants mostly from Western countries, who were selected using a selected sampling strategy that aimed to increase the detection power of the gene-environment interaction (Boks et al., 2007; Stringer et al., 2016). This could reduce the generalisability of the findings. Important to note is that this thesis used a retrospective self reported questionnaire as a measure of trauma. Although this tool was validated, it is still cause of concern due to the nature of self report tests. Adding to that is the small effect sizes displayed in the study. As seen in most other studies using PRS, we based our conclusions on relatively small effect sizes. Although having based our results on the latest GWAS (Cross-Disorder Group of the psychiatric Genomics Consortium, 2014), the SZ-PRS only explains a limited part of the SZ phenotype (nearing 7 %). thus making the results weak to modest at best.

Implications and Suggestions for Future Research

We would recommend further studies to incorporate samples with a more diverse genetic background and culture to see whether the results are reproducible in non-Western

environments. Furthermore, it could be interesting to look at the personality traits of non-diagnosed, high SZ-PRS individuals in a longitudinal setting to investigate whether their personality traits tend to shift towards the typical personality profile displayed in individuals with schizophrenia over time. It would also be interesting to investigate whether the current results are replicable with samples that have each experienced different types of CT. Lastly, with our current findings we would advise correcting for age and gender in future research.

Conclusion

Overall this study added insight to the relationship between SZ-PRS and openness, conscientiousness, extraversion, agreeableness and neuroticism, and the mediating role of CT in this relationship in a non-diagnosed population. Furthermore, it added insight by investigating the role of CT in these relationships and controlling for age and sex. The findings indicate that SZ-PRS is positively associated with openness and neuroticism and negatively associated with conscientiousness and agreeableness. No association was found for extraversion. Furthermore, results indicate that CT fully mediates the relationship between SZ-PRS and agreeableness, extraversion and neuroticism and partially mediates the relationship between SZ-PRS and conscientiousness. No mediation was performed for openness due to the absence of a significant association with CT, thereby eliminating the possibility of a significant mediation effect. Moreover, age and sex indicate to be significant covariates on all analyses with few exceptions, highlighting their importance in the current study. Additional research is needed to support the current findings, but our results indicate that a genetic predisposition for developing schizophrenia influences the development of personality traits through the mechanisms of CT even before a clinical diagnosis.

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Appendix - A (Additional Statistical Information)

VIF Values

Table 1A

The Effect of SZ-PRS on the Five Personality Traits Using a Linear Regression Whilst Controlling for Age and Sex

Variables	VIF
Openness	1.001
Conscientiousness	1.001
Extraversion	1.001
Agreeableness	1.001
Neuroticism	1.001

Note. $N = 910$

Table 2A

The Effect of SZ-PRS on the Five Personality Traits Using a Linear Regression Whilst adding Age, Sex and CT as Covariates

Variables	VIF
Openness	1.015
Childhood Trauma	1.020
Conscientiousness	1.015
Childhood Trauma	1.020
Extraversion	1.015
Childhood Trauma	1.020
Agreeableness	1.015
Childhood Trauma	1.020

Neuroticism	1.015
Childhood Trauma	1.020

Note. N =920

Table 3A

The Effect of SZ-PRS on Personality Traits Controlled for Age and Sex

Personality Traits	*B*	*t*	*p*	*R-squared*
Openness	.083	2.326	.020	.025
Conscientiousness	-.112	-2.681	.007	.052
Extraversion	-.073	-1.760	.079	.005
Agreeableness	-.070	-2.065	.039	.094
Neuroticism	.361	2.389	.017	.033

Note. N = 910

Table 4A

The Effect of SZ-PRS on CT Controlled for Age and Sex

Variable	*B*	*t*	*p*	*R-squared*
Childhood Trauma	.183	3.515	<.001	.019

Note. N = 910

Table 5A

The Effect of CT on Personality Traits Controlled for Age and Sex

Personality Traits	*B*	*t*	*p*	*R-squared*
Openness (O)	.026	1.144	.253	.021
Conscientiousness (C)	-.168	-6.443	<.001	.087

Extraversion (E)	-.192	-7.538	<.001	.061
Agreeableness (A)	-.226	-11.214	<.001	.201
Neuroticism (N)	1.215	13.902	<.001	.200

Note. N = 910

Table 6A

The effects of SZ-PRS on C Mediated by CT, controlled for age and sex

Analysis	*B*	*t*	*p*	*R-sq*	*F*	*LLCI*	*ULCI*
Direct Effect	-.0826	-2.0004	.0458	.0524	16.7100	-.1637	-.0016
Indirect Effect	-.0296	-	-	.0524	16.7100	-.0510	-.0122
Total Effect	-.1122	-2.6811	.0075	.0524	16.7100	-.1944	-.0301

Note. LLCI = Lower Limit Confidence Interval, ULCI = Upper Limit Confidence Interval. N = 910.

Table 7A

The effects of SZ-PRS on E Mediated by CT, controlled for age and sex

Analysis	*B*	*t*	*p*	*R-sq*	*F*	*LLCI*	*ULCI*
Direct Effect	-.0382	-.9431	.3459	.0054	1.6520	-.1178	.0413
Indirect Effect	-.0347	-	-	.0054	1.6520	-.0605	-.0144
Total Effect	-.0729	-1.7600	.0787	.0054	1.6520	-.1542	.0084

Note. LLCI = Lower Limit Confidence Interval, ULCI = Upper Limit Confidence Interval. N = 910

Table 8A

The effects of SZ-PRS on A Mediated by CT, controlled for age and sex

Analysis	*B*	*t*	*p*	*R-sq*	*F*	*LLCI*	*ULCI*
Direct Effect	-.0289	-.9035	.3665	.0944	31.4842	-.0915	.0338

Indirect Effect	-.0409	-	-	.0944	31.4842	-.0658	-.0194
Total Effect	-.0697	-2.0649	.0392	.0944	31.4842	-.1360	-.0035

Note. LLCI = Lower Limit Confidence Interval, ULCI = Upper Limit Confidence Interval. N = 910

Table 9A

The effects of SZ-PRS on N Mediated by CT, controlled for age and sex

Analysis	*B*	*t*	*p*	*R-sq*	*F*	*LLCI*	*ULCI*
Direct Effect	.1412	1.0178	.3090	.0359	11.2371	-.1310	.4134
Indirect Effect	.2203	-	-	.0359	11.2371	.1005	.3509
Total Effect	.3614	2.3894	.0171	.0359	11.2371	.0646	.6583

Note. LLCI = Lower Limit Confidence Interval, ULCI = Upper Limit Confidence Interval. N = 910

Table 10A

Test of Normality, Shapiro-Wilk

Variable	*p*
Age	<.001
Sex	<.001
SZ-PRS	.821
CTQ	<.001
Openness	.006
Conscientiousness	<.001
Extraversion	<.001
Agreeableness	<.001
Neuroticism	<.001

Note. N = 910

Table 11A

Additional Statistical Information Regarding the Age and Sex in Multiple Different Analyses

	Age		Sex	
Analysis	*B*	*p*	*B*	*p*
SZ-PRS on openness	.179	.045	1.364	<.001
SZ-PRS on conscientiousness	.300	.004	-2.651	<.001
SZ-PRS on extraversion	-.141	.172	.059	.894
SZ-PRS on agreeableness	.267	.001	-3.253	<.001
SZ-PRS on neuroticism	-.393	.296	-8.393	<.001
SZ-PRS on CT	.228	.078	-.962	.083
CT on openness	.173	.054	1.420	<.001
CT on conscientiousness	.339	<.001	-2.845	<.001
CT on extraversion	-.097	.335	-.141	.742
CT on agreeableness	.319	<.001	-3.481	<.001
CT on neuroticism	-.672	.051	1.420	<.001
SZ-PRS on conscientiousness with CT	.337	.001	-2.806	<.001
SZ-PRS on extraversion with CT	-.098	-.974	-.124	-.287
SZ-PRS on agreeableness with CT	.318	<.001	-3.467	<.001
SZ-PRS on neuroticism with CT	-.668	.052	-7.235	<.001
Mediation analysis for conscientiousness	.337	.001	-2.806	<.001
Mediation analysis for extraversion	-.098	.331	-.124	.774
Mediation analysis for agreeableness	.318	<.001	-.3468	<.001
Mediation analysis for neuroticism	-.668	.052	-7.235	<.001

Note. $N = 910$

Appendix - B (Syntax)

Spss Syntax - Appendix B

The Syntax has been divided into several parts that align with the analyses resulting in a better overview. When run the Syntax will also display the Histograms for normality checks.

Descriptives

```
DATASET ACTIVATE DataSet1.
FREQUENCIES VARIABLES=age sex
  /STATISTICS=STDDEV MINIMUM MAXIMUM MEAN
  /ORDER=ANALYSIS.
```

Linear Regressions H1

```
REGRESSION
  /MISSING LISTWISE
  /STATISTICS COEFF OUTS R ANOVA
  /CRITERIA=PIN(.05) POUT(.10)
  /NOORIGIN
  /DEPENDENT NEO_O
  /METHOD=ENTER SZ_0.5 age sex
  /SCATTERPLOT=(*ZPRED ,*ZRESID)
  /RESIDUALS HISTOGRAM(ZRESID).

REGRESSION
  /MISSING LISTWISE
  /STATISTICS COEFF OUTS R ANOVA
```

```
  /CRITERIA=PIN(.05) POUT(.10)
  /NOORIGIN
  /DEPENDENT NEO_C
  /METHOD=ENTER SZ_0.5 age sex
  /SCATTERPLOT=(*ZPRED ,*ZRESID)
  /RESIDUALS HISTOGRAM(ZRESID).

REGRESSION
  /MISSING LISTWISE
  /STATISTICS COEFF OUTS R ANOVA
  /CRITERIA=PIN(.05) POUT(.10)
  /NOORIGIN
  /DEPENDENT NEO_E
  /METHOD=ENTER SZ_0.5 age sex
  /SCATTERPLOT=(*ZPRED ,*ZRESID)
  /RESIDUALS HISTOGRAM(ZRESID).

REGRESSION
  /MISSING LISTWISE
  /STATISTICS COEFF OUTS R ANOVA
  /CRITERIA=PIN(.05) POUT(.10)
  /NOORIGIN
  /DEPENDENT NEO_A
  /METHOD=ENTER SZ_0.5 age sex
  /SCATTERPLOT=(*ZPRED ,*ZRESID)
```

```
  /RESIDUALS HISTOGRAM(ZRESID).


REGRESSION
  /MISSING LISTWISE
  /STATISTICS COEFF OUTS R ANOVA
  /CRITERIA=PIN(.05) POUT(.10)
  /NOORIGIN
  /DEPENDENT NEO_N
  /METHOD=ENTER SZ_0.5 age sex
  /SCATTERPLOT=(*ZPRED ,*ZRESID)
  /RESIDUALS HISTOGRAM(ZRESID).
```

Linear Regression H2

```
REGRESSION
  /MISSING LISTWISE
  /STATISTICS COEFF OUTS R ANOVA
  /CRITERIA=PIN(.05) POUT(.10)
  /NOORIGIN
  /DEPENDENT JTV_tot
  /METHOD=ENTER SZ_0.5 age sex
  /SCATTERPLOT=(*ZPRED ,*ZRESID)
  /RESIDUALS HISTOGRAM(ZRESID).
```

Linear Regressions H3

```
REGRESSION
  /MISSING LISTWISE
  /STATISTICS COEFF OUTS R ANOVA
  /CRITERIA=PIN(.05) POUT(.10)
  /NOORIGIN
  /DEPENDENT NEO_O
  /METHOD=ENTER age sex JTV_tot
  /SCATTERPLOT=(*ZPRED ,*ZRESID)
  /RESIDUALS HISTOGRAM(ZRESID).

REGRESSION
  /MISSING LISTWISE
  /STATISTICS COEFF OUTS R ANOVA
  /CRITERIA=PIN(.05) POUT(.10)
  /NOORIGIN
  /DEPENDENT NEO_C
  /METHOD=ENTER age sex JTV_tot
  /SCATTERPLOT=(*ZPRED ,*ZRESID)
  /RESIDUALS HISTOGRAM(ZRESID).

REGRESSION
  /MISSING LISTWISE
  /STATISTICS COEFF OUTS R ANOVA
  /CRITERIA=PIN(.05) POUT(.10)
  /NOORIGIN
```

```
  /DEPENDENT NEO_E
  /METHOD=ENTER age sex JTV_tot
  /SCATTERPLOT=(*ZPRED ,*ZRESID)
  /RESIDUALS HISTOGRAM(ZRESID).

REGRESSION
  /MISSING LISTWISE
  /STATISTICS COEFF OUTS R ANOVA
  /CRITERIA=PIN(.05) POUT(.10)
  /NOORIGIN
  /DEPENDENT NEO_A
  /METHOD=ENTER age sex JTV_tot
  /SCATTERPLOT=(*ZPRED ,*ZRESID)
  /RESIDUALS HISTOGRAM(ZRESID).

REGRESSION
  /MISSING LISTWISE
  /STATISTICS COEFF OUTS R ANOVA
  /CRITERIA=PIN(.05) POUT(.10)
  /NOORIGIN
  /DEPENDENT NEO_N
  /METHOD=ENTER age sex JTV_tot
  /SCATTERPLOT=(*ZPRED ,*ZRESID)
  /RESIDUALS HISTOGRAM(ZRESID).
```

Linear Regression Test for Possible Mediation

```
REGRESSION
  /MISSING LISTWISE
  /STATISTICS COEFF OUTS R ANOVA
  /CRITERIA=PIN(.05) POUT(.10)
  /NOORIGIN
  /DEPENDENT NEO_C
  /METHOD=ENTER age sex JTV_tot SZ_0.5
  /SCATTERPLOT=(*ZPRED ,*ZRESID)
  /RESIDUALS HISTOGRAM(ZRESID).

REGRESSION
  /MISSING LISTWISE
  /STATISTICS COEFF OUTS R ANOVA
  /CRITERIA=PIN(.05) POUT(.10)
  /NOORIGIN
  /DEPENDENT NEO_E
  /METHOD=ENTER age sex JTV_tot SZ_0.5
  /SCATTERPLOT=(*ZPRED ,*ZRESID)
  /RESIDUALS HISTOGRAM(ZRESID).

REGRESSION
  /MISSING LISTWISE
  /STATISTICS COEFF OUTS R ANOVA
  /CRITERIA=PIN(.05) POUT(.10)
```

```
  /NOORIGIN
  /DEPENDENT NEO_A
  /METHOD=ENTER age sex JTV_tot SZ_0.5
  /SCATTERPLOT=(*ZPRED ,*ZRESID)
  /RESIDUALS HISTOGRAM(ZRESID).

REGRESSION
  /MISSING LISTWISE
  /STATISTICS COEFF OUTS R ANOVA
  /CRITERIA=PIN(.05) POUT(.10)
  /NOORIGIN
  /DEPENDENT NEO_N
  /METHOD=ENTER age sex JTV_tot SZ_0.5
  /SCATTERPLOT=(*ZPRED ,*ZRESID)
  /RESIDUALS HISTOGRAM(ZRESID).
```

Linear Regressions using PROCESS to test for Mediation

The Syntax for these analyses will not be listed due to each analysis consisting of 5500+ lines worth of Syntax. Instead the following information will be given:

Y Variable: Neo_total_C

X Variable: SZ_0.5

Mediator(s) M: JTV_tot

Covariate(s): Sex, age

Model number: 4

Confidence intervals: 95

Number of bootstrap samples: 5000

Options: ‘Show total effect model (only models 4, 6, 80, 81, 82)’ and ‘ Effect size (mediation-only models)’

Y Variable: Neo_total_E

X Variable: SZ_0.5

Mediator(s) M: JTV_tot

Covariate(s): Sex, age

Model number: 4

Confidence intervals: 95

Number of bootstrap samples: 5000

Options: ‘Show total effect model (only models 4, 6, 80, 81, 82)’ and ‘ Effect size (mediation-only models)’

Y Variable: Neo_total_A

X Variable: SZ_0.5

Mediator(s) M: JTV_tot

Covariate(s): Sex, age

Model number: 4

Confidence intervals: 95

Number of bootstrap samples: 5000

Options: ‘Show total effect model (only models 4, 6, 80, 81, 82)’ and ‘ Effect size (mediation-only models)’

Y Variable: Neo_total_N

X Variable: SZ_0.5

Mediator(s) M: JTV_tot

Covariate(s): Sex, age

Model number: 4

Confidence intervals: 95

Number of bootstrap samples: 5000

Options: ‘Show total effect model (only models 4, 6, 80, 81, 82)’ and ‘ Effect size (mediation-only models)’

```
DESCRIPTIVES VARIABLES=SZ_0.5 JTV_tot NEO_O NEO_C NEO_E NEO_A NEO_N
  /STATISTICS=MEAN STDDEV MIN MAX.

DATASET ACTIVATE DataSet1.
EXAMINE VARIABLES=age sex SZ_0.5 JTV_tot NEO_O NEO_C NEO_E NEO_A
NEO_N
  /PLOT BOXPLOT HISTOGRAM NPPLOT
  /COMPARE GROUPS
  /STATISTICS DESCRIPTIVES
  /CINTERVAL 95
  /MISSING LISTWISE
  /NOTOTAL.
```