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Association between a serotonin transporter promoter polymorphism (5-HTTLPR) and personality disorder traits in a community sample

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Abstract

Background—The serotonin transporter (SERT) polymorphism (5HTTLPR) has been reported to be associated with several psychiatric conditions. Specific personality disorders could be intermediate factors in the known relationship between 5HTTLPR and psychiatric disorders. This is the first study to test the association between this polymorphism and dimensions of all DSM-IV personality disorders in a community sample.

Methods—374 white participants were assessed by clinical psychologists using the International Personality Disorder Examination (IPDE). Associations between dimensions of each DSM-IV personality disorder and the long (l) and short (s) alleles of the 5HTTLPR were evaluated using nonparametric tests and regression models.

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Results—The *s* allele of the 5HTTLPR polymorphism was significantly associated with higher avoidant personality trait scores in the whole sample. Males with the *s* allele had a significantly lower likelihood of higher obsessive-compulsive personality disorder (OCPD) trait scores, whereas females with the *s* allele were likely to have higher OCPD personality trait scores.

Conclusion—This paper provides preliminary data on the relationship between personality disorders and the 5HTTLPR polymorphism. The relationship of the *s* allele and avoidant PD is consistent with findings of a nonspecific relationship of this polymorphism to anxiety and depressive disorders. Concerning the unusual sexual dimorphic result with OCPD, several hypotheses are presented. These findings need further replication, including a more detailed study of additional variants in SERT.

Keywords

personality disorders; serotonin transporter gene; avoidant personality; obsessive compulsive personality; sex differences; polymorphism

1. Introduction

Personality disorders are maladaptive and inflexible enduring patterns of perceiving, relating to, and thinking about the environment and oneself, which are exhibited in a wide range of social and personal contexts. These disorders are egosyntonic, cause functional impairment and distress and are relatively stable over time (APA, 1994). To diagnose personality disorders pathological personality traits are assessed. However, these traits typically form a continuous distribution in populations, with no obvious point of rarefaction that would indicate the disorder definition (Livesley et al., 1998; Nestadt et al., 1992). Personality disorders are reported to have a substantial genetic basis (Kendler et al., 2008; Reichborn-Kjennerud, 2010). Results from family studies indicate familial aggregation of personality disorder traits (Asarnow et al., 2001; Hicks et al., 2004; McGirr et al., 2009; Reich, 1989). In addition, from twin studies the estimated heritabilities of individual personality disorders range from 21 to 79% (Coolidge et al., 2001; Kendler et al., 2006; Reichborn-Kjennerud et al., 2007; Torgersen et al., 2000).

The most comprehensively studied genetic variant in psychiatry is a polymorphism in the promoter region of the serotonin transporter gene (SLC6A4), designated as 5HTTLPR (Caspi et al., 2010; Murphy et al., 2004). The SLC6A4 gene is located on chromosome 17q11.1–17q12, and the encoded protein is an important target of selective serotonin reuptake inhibitors (SSRIs) (Ramamoorthy et al., 1993). Typically, there are two length polymorphisms of 5HTTLPR: a “short” (*s*) allele, with 14 repeats; and a “long” (*l*) allele, with 16 repeats. The *s* allele exhibits lower gene expression, resulting in reduced serotonin transporter (5HTT) expression and serotonin uptake in cells expressing that protein, including neurons, glia, blood platelets, and lymphoblasts (Heils et al., 1996; Greenberg et al., 1999).

The 5HTTLPR polymorphism has been found to be associated with several psychiatric disorders, including affective disorders (Collier et al., 1996), obsessive-compulsive disorder (Bloch et al., 2008), eating disorders (Calati et al., 2010), substance use disorders (Weizman & Weizman, 2000), and attention deficit disorder (Gizer et al., 2009). Moreover, a systematic review ($n=2,539$) suggested a positive association between the *s* variant and suicidal behavior ($p=0.009$) (Anguelova et al., 2003). In 1996, Lesch et al. first reported an association between the *s*-allele and anxiety-, depression- and aggression related general personality traits, using the NEO Personality Inventory (Lesch et al., 1996). Results from a large meta-analysis ($n=5,629$) reported suggestive evidence of an association between the *s*

allele and anxiety-related personality trait scores ($p=0.087$) as measured by several personality inventories; an especially strong association was found between the polymorphism and NEO neuroticism ($p<0.0001$) (Sen et al., 2004).

However, the relationship between pathologic personality traits, as defined by DSM-III or DSM-IV, and the 5HTTLPR has not been well-studied. Most papers have restricted their focus to a few personality disorders. The *s* allele has been reported to be associated with antisocial personality disorder traits (Garcia et al., 2010; Lyons-Ruth et al., 2007; Reese et al., 2010) and borderline personality disorder traits (Garcia et al., 2010), although findings have been inconsistent (Ishiguro et al., 1999; Liao et al., 2004; Pascual et al., 2008; Ni et al., 2006). Two studies reported association between the *l* allele and higher schizotypal personality traits (Golimbet et al., 2009; Golimbet et al., 2003). The only study of the relationship between obsessive-compulsive personality and the 5HTTLPR polymorphism failed to find an association (Perez et al., 2006). To the best of our knowledge, no study has investigated the association of the variants of the serotonin transporter gene with all personality disorders.

The aim of the current study was to explore the association of the 5HTTLPR polymorphism and all personality disorders as described in DSM-IV in a community sample from the Hopkins Epidemiology of Personality Disorders Study (HEPS) (Samuels et al., 2002). Since 5HTTLPR allele frequencies have been reported to differ by race (Gelernter et al., 1997; Gelernter et al., 1998), we restricted the current analyses to white participants. In addition, as there is evidence that sex modulates the influence of the 5HTTLPR on affective functioning (Stoltenberg & Vandever, 2010; Brummett et al., 2008b), we conducted sex-specific analyses.

2. Methods

2.1. Study Sample

Subjects participating in the Hopkins Epidemiology of Personality Disorder Study (HEPS) were sampled from the Baltimore Epidemiologic Catchment Area (ECA), which has been described previously (Eaton et al., 1997; Eaton et al., 1998). In brief, 3481 subjects were interviewed in 1981, comprising the Eastern Baltimore Mental Health Survey of the ECA. Between 1993 and 1996, 1920 subjects (73% of the surviving sample) were re-interviewed, as part of the Baltimore ECA Follow-up survey. From these individuals, all those who were examined by psychiatrists in 1981, as well as all subjects who were identified by the Diagnostic Interview Survey (DIS) as having a lifetime diagnosis of mania, depression, panic disorder, obsessive-compulsive disorder, alcohol use disorder, or drug use disorder at follow up. In addition, a 25% (222/884) random sample was selected from the remaining subjects. A total of 742 subjects completed the personality examination between 1997 and 1999 in the HEPS study (Samuels et al., 2002) reported in this paper. The study was approved by the Institutional Review Board of Johns Hopkins Medical Institutions. Prior to the interview, participants provided informed consent for study procedures, including the interview and collection of a DNA sample.

2.2. Clinical Assessment

DSM-IV personality disorder traits were assessed by four masters-level clinical psychologists using the International Personality Disorder Examination (IPDE) between 1997 and 1999. The IPDE is a validated semi-structured interview with demonstrated inter-rater reliability and temporal stability used to diagnose personality disorders (Loranger et al., 1994). All DSM-IV personality disorders were evaluated. Each trait was rated absent (0), accentuated or exaggerated (1), criterion level (2) or missing / unknown (9). To obtain

additional information, the subjects' relative or friend was interviewed. In forty jointly rated interviews, the intraclass correlation coefficients for number of DSM-IV personality criteria rated 1 or 2 were: schizoid (0.81), schizotypal (0.58), paranoid (0.63), antisocial (0.80), borderline (0.76), histrionic (0.62), narcissistic (0.62), avoidant (0.89), dependent (0.76), and obsessive-compulsive (0.70). Psychiatric evaluations were conducted by five psychiatrists who examined participants using an adapted version of the Schedule for Clinical Assessment in Neuropsychiatry (SCAN, version 1.5) (Wing et al., 1990) for current and lifetime disorders according to DSM-IV criteria (APA, 1994).

2.3. Genotyping

HEPS participants were sampled by venous blood or cheek swab if they did not want to provide a venous sample. Subjects who agreed to provide DNA were sampled by finger-stick onto a specially formulated "Isocode" Card. DNA was isolated from peripheral blood leukocytes using Puregene Blood Kit chemistry on an Autopure LS automated DNA purification instrument (Qiagen, Valencia, Calif). Buccal swabs were isolated manually using a Puregene DNA isolation kit (Qiagen) following manufacturer's protocol. Blood collected on Isocode Cards was isolated according to the manufacturer's instructions by heating hole punches (made by the American Red Cross) in distilled water at 95°C for 30 minutes. DNA concentrations were determined by spectrophotometry using a DU 530 Life Science UV/Vis Spectrophotometer (Beckman Coulter, Brea, California). The 5HTTLPR genotype was determined by polymerase chain reaction amplification (polymerase chain reaction primers and conditions are available upon request).

A total of 628 (85%) of the 742 participants provided a blood sample and were genotyped for 5HTTLPR. The 114 un-genotyped subjects had similar distributions of race, age, sex and marital status and had more years of education compared to genotyped subjects; however, the level of education was not related to the 5HTTLPR allele distribution. The distribution of 5HTTLPR genotypes was "s/s", 74 (11.8%); "s/l", 274 (43.6%); and "l/l", 280 (44.6%), and was in Hardy Weinberg equilibrium ($\chi^2_1 = 0.31$, $p > 0.5$) (Rodriguez et al., 2009).

Earlier studies reported that 5HTTLPR polymorphism allele frequencies differ by race (Gelernter et al., 1997; Gelernter et al., 1998). Based on self-reported race or ethnicity, the study sample consisted of 376 white individuals (59.9%), 232 African-Americans (36.9%), 6 Hispanics (1.0%), 2 Asians (0.3%), 1 Pacific Islander (0.2%) and 11 individuals with other race or ethnicities (1.8%). The genetic race corresponded highly with the self-reported race, as described earlier (Reti et al., 2011). The polymorphism frequencies of the white participants subsample differed significantly from the rest of the sample ($\chi^2_2 = 26.93$, $p < 0.0001$), and this paper only presents the results for the white individuals.

Based on the evaluation of the 5HTTLPR's short allele's functional effect in vitro and in vivo (Bennett et al., 2002; Lesch et al., 1996), l/s and s/s genotypes were combined in the s-group and compared to the l/l genotype, the l-group.

2.4 Statistical Analyses

Ten personality disorder dimensional scores were calculated by summing the ratings (0, 1, or 2) for the individual traits comprising each disorder. A non-parametric test, the Mann-Whitney U test, was used to compare personality disorder scores between the s and l groups. For personality disorders that were significantly different between groups, then the frequency distribution of personality disorder score categories (0, 1–2, 3–4, or 5+) between the s and l groups were compared. The odds ratio (OR) and 95% confidence interval (95% CI) were estimated for the relationship between genotype and personality disorder score using ordinal regression, with the genotype as independent variable and personality disorder

score categories as dependent variables. Finally, we estimated the magnitude of the relationships between genotype group and specific personality disorder traits using logistic regression. The specific personality traits were marked present, when they had been rated '1' or '2'. Analyses were performed on the entire sample, and then stratified by sex. Unadjusted and adjusted relationships were estimated; in adjusted models, current major depression and current anxiety disorder (which included agoraphobia, panic disorder, social phobia, or OCD) were included as covariates. In this exploratory analysis a p-value threshold of 0.05 was considered significant. Predictive Analytic Software (PWAS) for Windows version 18.0 was used to conduct the analyses (SPSS inc, Chicago, IL, 2010).

3. Results

3.1. Sample Characteristics

Of the 376 Caucasian American participants, 216 (57%) subjects were female, and 160 (43%) were male. Their ages ranged from 34 through 94 years (mean 52.13, SD 13.53). The genotype frequencies were 52 's/s' (13.8%), 188 's/l' (50.0%) and 136 'l/l' (36.2%); i.e. 136 (36.2%) *l*-group and 240 (63.8%) *s*-group. In women, the genotype distribution was 31 's/s' (14.4%), 104 's/l' (48.1%) and 81 'l/l' (35.5%). In men, the genotype distribution was 21 's/s' (13.1%), 84 's/l' (52.5%) and 55 'l/l' (34.4%). The genotype frequencies did not differ by sex ($\chi^2_2 = 0.696$, $p=0.706$).

3.2. Relationship between polymorphism and PD trait scores

Table 1 shows personality disorder trait score means and standard deviations by 5HTTLPR genotype group. The mean number of avoidant personality traits was significantly higher ($p=0.017$) in subjects carrying the *s* allele compared to the non *s*-allele carriers. There was no association between the polymorphism and any other PD score. In the post-hoc analysis, the relation between avoidant personality traits was further investigated using ordinal regression (Table 2). The results remained significant. The presence of the *s* allele was associated with significantly higher avoidant personality trait scores (OR 1.63 95%CI 1.07–2.48, Wald test 5.14, df1, $p=0.023$). Controlling for major depressive disorder and any anxiety disorder, the association remained significant (OR 1.54 95%CI 1.00–2.32, Wald test 3.88, df1, $p=0.049$).

3.3. Obsessive Compulsive Personality: sex specific results

Table 1 also shows personality disorder trait score means and standard deviations by 5HTTLPR genotype group, stratified by sex. Mean obsessive-compulsive personality (OCP) scores were statistically significantly higher in men in the *l*-group ($p=0.011$), while there was a trend for higher OCP scores in women in the *s*-group ($p=0.075$). This opposite effect across sexes was accentuated when we performed post hoc analyses in ordinal regression models (Table 3). Male *s*-allele carriers had statistically significantly lower OCP trait scores (OR 0.47, 95%CI 0.25–0.84, Wald test 6.37, df1, $p=0.012$) whereas female *s* allele carriers had slightly higher OCP trait scores (OR 1.61, 95%CI 0.97–2.67, Wald test 3.37, df1, $p=0.066$). The other personality traits did not show any significant differences across sexes. Controlling for major depressive disorder and any anxiety disorder the association became somewhat stronger in males (OR 0.44 95%CI 0.24–0.81 Wald 6.85, df1, $p=.009$) and weaker in females (OR 1.51 95%CI 0.91–2.55 Wald 2.68, df1, $p=0.102$).

To further analyze the sex-specific differences in obsessive-compulsive scores; individual OCP traits were investigated (Table 4). Traits were considered present when subjects scored 1 (accentuated or exaggerated) or 2 (criterion level). The traits *scrupulousness*, *perfectionism* and *reluctance to delegate* were significantly less common in males carrying the *s* allele (OR0.30 95%CI 0.14–0.66, Wald 8.99, df1, $p=0.003$; OR0.41 95%CI 0.20–0.82,

Wald 6.32, df1, $p=0.012$; OR 0.45 95%CI 0.22–0.91, Wald 4.91, df1, $p=0.027$, respectively). The magnitude of the associations for individual OCP traits were not appreciably changed when current major depression or anxiety disorders were included as covariates (data not shown but available upon request). Interestingly, seven out of eight traits tended to be more common in *s*-carrying women; whereas those same seven traits tended to be less common in *s*-carrying men.

All the above analyses were conducted using a score for each personality disorder trait of 1 or 2. When the data were reanalysed using only personality disorder trait scores of 2, the estimates of the significant ORs remained constant or became stronger, only the 95% CI broadened, which lowered the *p*-value (for avoidant as well as for obsessive-compulsive personality).

Discussion

To the best of our knowledge, this is the first community-based study to explore associations of the serotonin transporter polymorphism with traits from all 10 personality disorders. First, we found that the *s* allele is associated with significantly higher avoidant personality trait scores; the relationship appeared particularly strong in women. Second, we did not find a relationship between the polymorphism and OCPD in unstratified analyses, because the variants appeared to have opposite effects in men and women. Male *s* allele carriers had significantly lower OCPD trait scores whereas female *s* allele carriers tended to have higher OCPD personality trait scores. Remarkably, these sex-specific results were consistent for the individual traits; seven out of eight OCPD traits were associated with the *l* allele in men (three significantly so), while women with the *s* allele tended to score higher on these same seven OCPD criteria.

Other than for avoidant and obsessive-compulsive, we did not find a relation between pathological personality disorder trait scores and the 5HTTLPR. Although the literature is inconsistent, some studies report evidence for a relationship between the 5HTTLPR polymorphism and other personality disorders. Garcia et al. (2010) found an incremental effect for the combination of the 5HTTLPR *s* allele and 5-HTTVNTR 12/12 polymorphism in predicting antisocial personality disorder in 147 male inmates (Garcia et al., 2010). This is supported by a study of Lyons-Ruth, who found that the *s* allele was associated with borderline or antisocial personality disorders in a sample of 34 low-income young adults with borderline or antisocial personality disorder and 62 adults without these conditions (Lyons-Ruth et al., 2007). However, a Japanese study failed to provide supportive evidence for an association of the *s/s* genotype with severe alcoholism with antisocial behaviors (Ishiguro et al., 1999), and two other clinical studies did not find an association between the polymorphism and borderline personality (Ni et al., 2006; Pascual et al., 2008). Two Russian studies found that individuals with the 5-HTTLPR *s/s* genotype had lower scores on scales related to schizotypal personality traits (Golimbet et al., 2003; Golimbet et al., 2009).

A potential reason for the inconsistency between these findings and those of the current study may be the study designs. Most studies are done in clinical populations (Garcia et al., 2010; Golimbet et al., 2003; Lyons-Ruth et al., 2007), whereas this study is community based. Patients score higher on personality disorder scales than do persons selected from the general population (Livesley et al., 1998). Second, most studies use self-report inventories (Garcia et al., 2010; Golimbet et al., 2003; Golimbet et al., 2009) or trained interviewers (Lyons-Ruth et al., 2007) to measure personality disorders, whereas in this study personality interviews were conducted by clinical psychologists. As noted previously, such differences in assessment are associated with different personality disorder measurement properties (Perry, 1992).

In this study, avoidant personality traits are related to the *s* allele of the 5HTTLPR polymorphism. According to the literature, *s*-carriers exhibit high neuroticism (Lesch et al., 1996), a personality trait highly correlated with avoidant personality (Morey et al., 2002). Furthermore, it is reported that individuals carrying the *s* allele, demonstrate elevated amygdala reactivity in response to fearful stimuli (Hariri et al., 2002) and exhibit more depressive symptoms, major depression and suicidality after experiencing stressful life events (Caspi et al., 2003). In several large studies, individuals with avoidant personality show high rates of comorbid anxiety and mood disorders (Oldham et al., 1995; McGlashan et al., 2000). In a longitudinal cohort study, avoidant personality traits were a leading predisposing factor to subsequent first-onset panic disorder or agoraphobia (Bienvenu et al., 2009). As expected, when we controlled for anxiety and depression, the association of the *s* allele and avoidant personality traits was attenuated. Since avoidant traits appear to predispose persons to psychopathology, this is likely an example of “over-controlling,” as avoidant traits may mediate or be markers of risk for subsequent psychopathology.

In the current study, the *l* allele was significantly associated with obsessive-compulsive traits in males, especially the individual traits of perfectionism, reluctance to delegate, and scrupulosity, with four of the remaining five OCPD traits trending in the same direction. Conversely, the same seven obsessive-compulsive traits trended to be associated with the *s* allele in women. This finding is in contrast with a study conducted by Perez et al., who found no difference in frequencies of SERT variants between persons (undergraduate students and volunteers, $n=153$) with and without OCPD as measured with the SCID-II (Perez et al., 2006); no sex differences were reported. This negative finding could be explained by lack of power, different demographic profiles (predominantly female and young in the Perez et al. study), and disequilibrium in the distribution of the genotypes (the *l/l* group was in the minority in that study).

It is not clear why the association of the 5-HTT and obsessive compulsive personality traits is sex-specific, but the current finding is concordant with prior literature on sex-specific effects of the SERT polymorphism. Several studies found a sex-by-5-HTTLPR-by-environmental stress effect in depression; indicating that in females the *s* allele may increase an individual's susceptibility to depression under stressful life conditions (Jacobs et al., 2006; Gonda et al., 2005; Zalsman et al., 2006); while in males the *s* allele may not confer this susceptibility (Eley et al., 2004), or even be protective against the development of depression (Brummett et al., 2008a; Sjöberg et al., 2006). Two independent studies found that men with the 5-HTTLPR *s* variant reported lower anxiety, whereas women did not (Flory et al., 1999; Brummett et al., 2003).

Alternatively, it may be that OCPD manifests differently in men and women, despite both sexes meeting or experiencing the same OCPD criteria through examination. For instance, it is possible that men with OCPD are more similar to individuals with the broader phenotype of autism. This could be supported by a similar phenomenology in the disorders. That is, individuals with the broader autism phenotype and those with OCPD have similar traits, e.g. preoccupation with details, repetitive behaviors and rigidity (Bejerot et al., 2001; Gillberg & Billstedt, 2000). In addition, a family study by Piven et al. has suggested associations between obsessive compulsive personality behaviors in parents of autistic children and repetitive scales (Piven et al., 1997). Second, autism, as with many other neuropsychiatric disorders of childhood including attention-deficit hyperactivity disorder and Tourette syndrome, is predominantly diagnosed in males (Levy et al., 2009). Hence, a sex-specific neurodevelopmental vulnerability to multiple disorders may be manifested in some adults as OCPD traits in males. From a genetic perspective, Sutcliffe et al. found genetic linkage to autism to be increased in 17q11.2 which contains the *serotonin transporter* locus. In this study, 202 families containing only affected males (“male-only families”) (Sutcliffe et al.,

2005) were studied, raising the possibility of sex-specific genetic effects for susceptibility to autism at this locus. So it might be that the association of the 5HTTLPR *l*-allele with male patients, as opposed to females, might represent a particular OCPD phenotype.

Although the literature is sparse, OCPD traits have been associated with serotonergic dysfunction. Several studies propose an advantageous effect for selective serotonin reuptake inhibitors (SSRIs) in OCPD (Ekselius & Von, 1999; Ricciardi et al., 1992; Cavedini et al., 1997; Anseau et al., 1991). This is in accordance with research from Stein et al. which shows blunted fenfluramine-mediated prolactin-responses in OCPD (Stein et al., 1996). From a neurobiological point of view, sex-differences in serotonin function are a common phenomenon. For example, the effectiveness of SSRIs is lower in males than in females (Khan et al., 2005; Kornstein et al., 2000; Young et al., 2009), and increasing tryptophan levels increases negative affect in males carrying the 5-HTTLPR *l* allele, whereas this occurs for females carrying the *s* allele (Brummett et al., 2008b). Sex-differences in serotonin availability, receptor density and estrogen steroid serotonergic modulation have been examined as mediators of brain sex differences (Cosgrove et al., 2007). How these characteristics relate to sex differences in obsessive-compulsive traits remains unclear; however, the consistency of sex-differences in serotonergic function is remarkable.

The strengths of this study include the population-based design and the use of professional psychiatric interviewers to measure personality disorders. Several limitations must be mentioned. First, we have to be cautious about interpretation of the 5HTTLPR results because subjects were only genotyped for 5HTTLPR *s* and *l* alleles. That is, in 2006 a new single-nucleotide functional polymorphism was identified in the repeats region (rs25531). Rs25531 is almost always found in the *l* allele, and *l* alleles with one rs25531 variant and *s* alleles have equivalent expression levels, which are about half of that of the typical *l* allele (Hu et al., 2006). Nevertheless, the minor allele frequency of rs25531 in Caucasian subjects is estimated between 7–15% (Hu et al., 2006; Xie et al., 2009; Wendland et al., 2006). Second, results should be interpreted with caution given multiple testing considerations; results of this study must be viewed as exploratory. These data are a novel exploration of the association of the serotonin transporter polymorphism and pathologic personality traits and are intended to aid in hypothesis-generation for future studies. Third, the study subjects were originally recruited in 1981 into the Baltimore ECA project. Over time, the sample has been affected by aging and loss to follow-up. Comparison between participant and non-participant subjects has revealed only minor demographic differences other than age, but those with antisocial personality disorder were more frequently lost to follow-up (Samuels et al., 2002; Badawi et al., 1999). Thus, the negative findings relating to antisocial personality disorder may be due to reduced power. The last limitation of the study is that the analyses are based on personality disorder trait scores. Criterion counts provide a coarse estimation of one's PD trait level. Individual criteria may not be equally related to the latent construct as reported by (Cooper et al., 2010). Nevertheless, dimensional scores may be more appropriate than dichotomously diagnosed personality disorders when understanding personality pathology (Frances, 1982).

This paper yields interesting preliminary data with regard to the relationships between personality disorders and the serotonin transporter polymorphism. In summary, we found a relationship between the *s* allele and avoidant personality traits in a white community-based population. Second, this paper describes an association between the *l* allele and obsessive-compulsive traits in men, and a trend toward a similar association with the *s* allele in the women. We hypothesize that pathologic personality traits may mediate the relationship between 5HTTLPR genotypes and psychiatric illnesses. The study needs replication in another general population sample with genotyping of all 5HTTLPR variants and consideration of sex and race influences.

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Table 1

Personality disorder trait score means by 5HTTLPR genotype group

Personality disorder dimension	Total sample		Male subsample		Female subsample	
	S group (n=237) mean	L group (n=135) mean	S group (n=103) mean	L group (n=55) mean	S group (n=135) mean	L group (n=81) mean
Schizoid	0.91 (SD 1.61)	0.92 (SD 1.64)	0.92 (SD 1.64)	1.04 (SD 1.70)	1.58 (SD 1.59)	0.85 (SD 1.60)
Schizotypal	1.55 (SD 2.51)	1.51 (SD 2.26)	1.15 (SD 2.66)	1.82 (SD 2.82)	1.53 (SD 2.41)	1.29 (SD 1.76)
Paranoid	1.38 (SD 1.90)	1.31 (SD 1.84)	1.42 (SD 1.91)	1.71 (SD 2.27)	1.35 (SD 3.07)	1.05 (SD 1.43)
ASP adult	2.58 (SD 3.37)	2.29 (SD 3.04)	3.53 (SD 3.53)	3.67 (SD 3.38)	1.86 (SD 3.06)	1.35 (SD 2.37)
Borderline	2.44 (SD 2.87)	2.37 (SD 2.81)	2.36 (SD 2.53)	2.81 (SD 2.73)	2.49 (SD 3.12)	2.06 (SD 2.84)
Histrionic	1.13 (SD 2.01)	1.00 (SD 1.80)	1.02 (SD 1.91)	0.89 (SD 1.56)	1.22 (SD 2.09)	1.08 (SD 1.96)
Narcissistic	0.96 (SD 1.87)	1.19 (SD 2.14)	1.50 (SD 2.17)	1.67 (SD 2.35)	0.55 (SD 1.47)	0.86 (SD 1.94)
Avoidant	1.28 (SD 1.94)	1.03 (SD 2.28) ^a	1.19 (SD 1.83)	1.13 (SD 2.54)	1.35 (SD 2.04)	0.98 (SD 2.10) ^c
Dependent	0.95 (SD 1.68)	0.94 (SD 1.80)	0.66 (SD 1.19)	0.63 (SD 1.41)	1.18 (SD 1.95)	1.15 (SD 2.01)
Obsessive-compulsive	2.23 (SD 2.23)	2.38 (SD 2.57)	2.16 (SD 2.35)	3.34 (SD 3.03) ^b	2.29 (SD 2.39)	1.71 (SD 1.94)

^aMann-Whitney U p=0.017,

^bMann-Whitney U p=0.011,

^cMann-Whitney U p=0.057

Table 2
Association between avoidant personality disorder dimension and 5HTTLPR genotype group

Avoidant personality dimension score	Total sample		Male subsample		Female subsample	
	s-group	l-group	s-group	l-group	s-group	l-group
0	127 (53.1%)	88 (65.2%)	54 (51.9%)	36 (65.5%)	28 (26.9%)	9 (16.4%)
1–2	65 (27.2%)	29 (21.5%)	30 (28.8%)	11 (20.0%)	44 (42.3%)	19 (34.5%)
3–4	28 (11.7%)	10 (7.4%)	13 (12.5%)	5 (9.1%)	19 (18.3%)	12 (21.8%)
5+	19 (7.9%)	8 (5.9%)	7 (6.7%)	3 (5.5%)	13 (12.5%)	15 (27.3%)
OR*	OR 1.63 (95%CI 1.07–2.48) Wald 5.14, df1, p=0.023		OR 1.67 (95%CI 0.87–3.21) Wald 2.24, df1, p=0.125		OR 1.59 (95%CI 0.92–2.78) Wald 2.46, df1, p=0.097	

* L group is reference

Table 3
Association between obsessive-compulsive personality disorder dimension and 5HTTLPR genotype group

Obsessive-compulsive personality dimension score	Total sample		Male subsample		Female subsample	
	s-group	l-group	s-group	l-group	s-group	l-group
0	63 (26.4%)	41 (30.4%)	28 (26.9%)	9 (16.4%)	35 (25.9%)	32 (40.0%)
1–2	98 (41.0%)	43 (31.9%)	44 (42.3%)	19 (34.5%)	54 (40.0%)	24 (30.0%)
3–4	43 (18.0%)	29 (21.5%)	19 (18.3%)	12 (21.8%)	24 (17.8%)	17 (21.3%)
5+	35 (14.6%)	22 (16.3%)	13 (12.5%)	15 (27.3%)	22 (16.3%)	7 (8.8%)
OR *	OR 0.97 (95%CI 0.66–1.42) Wald 0.02, df1, p=0.882		OR 0.47 (95%CI 0.25–0.84) Wald 6.37, df1, p=0.012		OR 1.61 (95%CI 0.97–2.67) Wald 3.37, df1, p=0.066	

* L group is reference

Table 4

Association between individual obsessive-compulsive personality traits 5HTTLPR genotype group

	Male subsample	Female subsample
OCP traits male	OR (95%CI) *	OR (95%CI) *
Work devotion	1.20 (0.54–2.68)	0.92 (0.41–2.07)
Perfectionism	0.41 (0.20–0.82) ^a	1.31 (0.69–2.52)
Preoccupation details	0.52 (0.24–1.15)	1.76 (0.87–3.58)
Unable to discard	0.83 (0.41–1.69)	1.46 (0.74–2.89)
Scrupulousness	0.30 (0.14–0.66) ^b	1.57 (0.73–3.37)
Miserly	0.58 (0.19–1.69)	1.60 (0.55–4.67)
Reluctant to delegate	0.45 (0.22–0.91) ^c	1.41 (0.77–2.58)
Stubborn	0.62 (0.32–1.19)	1.36 (0.77–2.41)

* L group is reference

^a p<0.05,

^b p<0.01,

^c p<0.05