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Introduction

Associations between the common polymorphism in the serotonin transporter (5-HTT) promoter 5-HTTLPR and the personality traits Neuroticism and Harm Avoidance are equivocal. The temperamental trait Sensory Processing Sensitivity (SPS), which is characterized by increased sensitivity to environmental stimuli (Aron and Aron, 1997) and is related to Neuroticism and Openness (Smolewska et al., 2006), may describe an underlying characteristic more directly associated with 5-HTTLPR genotype. High levels of SPS are found in 15-20% of the population and have in fMRI studies been associated with enhanced neural processing of detailed visual stimuli (Jagiellovicz et al., 2011) and increased neural activation in response to happy and sad faces (Acedvedo et al., 2010). Several defining characteristics of SPS, as reflected by items on the self-report questionnaire, are similar to physiological characteristics found in 5-HTTLPR short allele carriers, including increased brain activation in response to emotional stimuli (Canli et al., 2005), increased acoustic startle response (Brocke et al., 2006), and increased cortisol response to social evaluation (Way et al., 2010). High levels of SPS may reflect an endophenotype associated with the 5-HTTLPR short/short genotype.

Methods

Participants

Two-hundred healthy adult individuals (aged 18-88), included in the Cimbi database between 2000 and 2010, completed NEO-PI-R and TCI personality batteries at the time of inclusion. Blood samples were collected and genotypes for the 5-HTTLPR polymorphism determined. In 2010, the cohort (n = 169, 58.6% male) completed the questionnaires Highly Sensitive Person (HSP) Scale and the Symptom Checklist-90R (SCL-90R).

Questionnaires

NEO-PI-R – The Revised NEO Personality Inventory, A 240-item self-report questionnaire providing a measure of the Five Factor Model: Neuroticism, Extraversion, Openness to Experience, Agreeableness, and Conscientiousness (Costa and McCrae, 1992).

Temperament and Character Inventory (TCI) A 240-item questionnaire providing a measure of four dimensions of temperament (Harm Avoidance, Novelty Seeking, Reward Dependence, and Persistence) and three of character (Cloninger et al., 1994).

Highly Sensitive Person (HSP) Scale. A 27-item self-report questionnaire providing a measure of Sensory Processing Sensitivity (HSP score) (Aron and Aron, 1997) and the three facets Aesthetic Sensitivity (AES), Ease of Excitation (EOE), and Low Sensory Threshold (LST) (Smolewska et al., 2006). Examples of questions: 'Do other people's moods affect you?', 'Do you startle easily?', and 'Does being very hungry create a strong reaction in you, disrupting your concentration or mood?' Items are rated on a 1-7 Likert scale, giving total scores in the range of 27-189. The present dataset has scores in the range of 27-138, mean ± SD of 92.6 ± 19.1, and a Cronbach's α of 0.86.

Revised Hopkins Symptom Checklist (SCL-90R). A 90-item self-report questionnaire providing a measure of symptoms of distress and psychopathology within the past week consisting of a Global Severity Index (GSI) and scores for nine sub-scales of psychopathology (Derogatis LR, 1994).

5-HTTLPR Genotyping

5-HTT gene-linked polymorphic region (5-HTTLPR, rs4795541). A 44 bp insertion/deletion in the promoter region of the 5-HTT gene giving rise to short (s) and long (l) alleles. Determined with a TaqMan 5'-exonuclease allelic discrimination assay and ABI 7500 multiplex PCR (Applied Biosystems). The three genotypes: ll (n = 55, 32.5%), sl (n = 82, 48.5%), and ss (n = 32, 18.9%) were in Hardy-Weinberg equilibrium (s allele frequency: 43%, $X^2 = 0.021$, p = 0.883).

Statistical analysis

Performed in GraphPad Prism 5.04, GraphPad InStat 3.10, and STATA/MP 10.1.

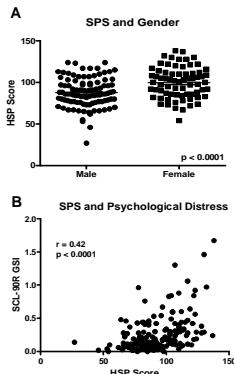


Figure 1. Influence of gender and psychological distress on Sensory Processing Sensitivity. A) Females have higher HSP score than males (99.8 ± 2.2 vs. 87.6 ± 1.8, p < 0.0001, Student's t test, n = 169). B) Global Severity Index (GSI) on the SCL-90R measure of psychological distress is positively correlated with HSP score (Spearman's $r = 0.42$, p < 0.0001, n = 165).

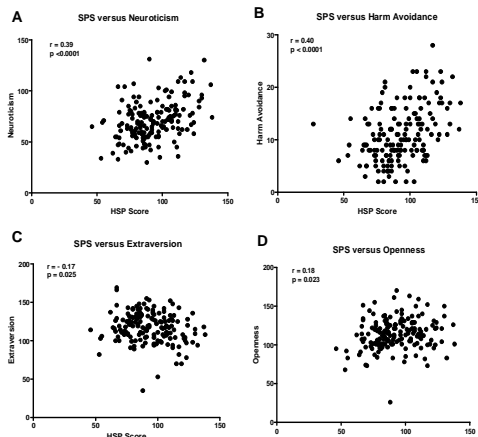


Figure 2. Correlations between Sensory Processing Sensitivity and associated personality traits. A) Neuroticism is correlated with HSP score (Pearson's $r = 0.39$, p < 0.0001). B) Harm Avoidance is correlated with HSP score (Spearman's $r = 0.40$, p < 0.0001). C) Extraversion is negatively correlated with HSP score (Pearson's $r = -0.17$, p = 0.025). D) Openness is correlated with HSP score (Pearson's $r = 0.18$, p = 0.023). Reward Dependence is correlated with HSP score (Pearson's $r = 0.26$, p = 0.0007, data not shown). n = 164-165.

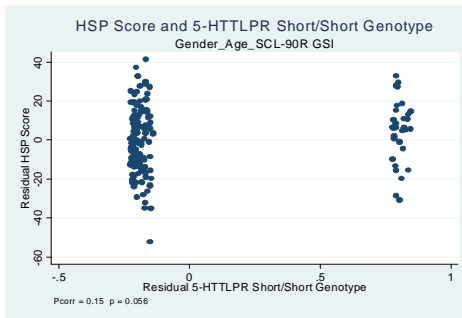


Figure 3. Sensory Processing Sensitivity is not associated with 5-HTTLPR Short/Short Genotype when taking gender, age, and psychological distress into account. Partial regression plot of HSP score vs. 5-HTTLPR s/s genotype (s/s = 1, s/l or l/l = 0), (pcorr = 0.15, p = 0.056). Model: adj. $R^2 = 27.4\%$, n = 164. 5-HTTLPR s/s: coeff. = 6.21, se = 3.23.

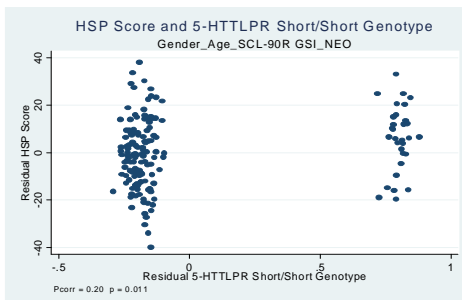


Figure 4. Sensory Processing Sensitivity is associated with 5-HTTLPR Short/Short Genotype when taking gender, age, psychological distress, and the personality traits Neuroticism, Extraversion, and Openness into account. Partial regression plot of HSP score vs. 5-HTTLPR s/s genotype (s/s = 1, s/l or l/l = 0), (pcorr = 0.20, p = 0.011). Model: adj. $R^2 = 38.4\%$, n = 161. 5-HTTLPR s/s: coeff. = 7.56, se = 2.93.

	5-HTTLPR Short/Short	5-HTTLPR Short Allele Carrier
Sensory Processing Sensitivity	0.15 (p = 0.056)	na
Neuroticism	-0.04 (p = 0.628)	0.03 (p = 0.704)
Harm Avoidance	-0.10 (p = 0.202)	-0.10 (p = 0.210)
Sensory Processing Sensitivity (Neuroticism)	0.18 (p = 0.026)*	na
Sensory Processing Sensitivity (Harm Avoidance)	0.18 (p = 0.025)*	na
Neuroticism (Sensory Processing Sensitivity)	-0.08 (p = 0.325)	na
Harm Avoidance (Sensory Processing Sensitivity)	-0.15 (p = 0.066)	na
Sensory Processing Sensitivity (Neu., Ext., Op.c.)	0.20 (p = 0.011)*	na

Table 1. Comparison of associations of Sensory Processing Sensitivity, Neuroticism, and Harm Avoidance with 5-HTTLPR Short allele. Values are partial correlation coefficients for 5-HTTLPR short allele status with each personality trait taking gender, age (SPS only), and psychological distress (SCL-90R GSI) into account. Models in bottom section include the personality traits listed in parentheses to test each personality trait's association with 5-HTTLPR s/s genotype independent of associated traits. n = 161-164. * p < 0.05.

	Total HSP	AES	EOE	LST
Neuroticism	0.39***	0.10	0.42***	0.30***
Extraversion	-0.17*	0.15	-0.24**	-0.27***
Openness	0.18*	0.47***	-0.01	-0.08
Conscientiousness	-0.01*	-0.02*	-0.04*	-0.10*
Agreeableness	0.12*	0.07*	0.06*	0.17**

Table 2. Correlations between Sensory Processing Sensitivity facets and personality traits of the Five Factor Model. The facets Ease of Excitation (EOE) and Low Sensory Threshold (LST) are correlated with Neuroticism and negatively correlated with Extraversion. The facet Aesthetic Sensitivity (AES) is correlated with Openness. Values are Pearson's correlation coefficients. *Spearman correlation coefficient. n = 165. * p < 0.05, ** p < 0.01, *** p < 0.001.

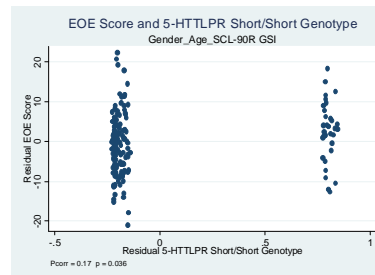


Figure 5. Ease of Excitation (EOE) is associated with 5-HTTLPR Short/Short Genotype when taking gender, age, and psychological distress into account. Partial regression plot of EOE score vs. 5-HTTLPR s/s genotype (s/s = 1, s/l or l/l = 0), (pcorr = 0.17, p = 0.036). Model: adj. $R^2 = 30.0\%$, n = 164. 5-HTTLPR s/s: coeff. = 3.25, se = 1.54.

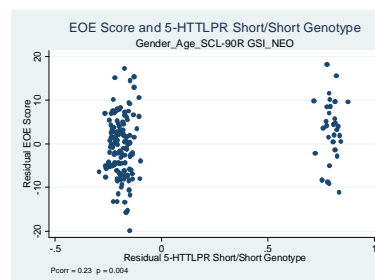


Figure 6. Ease of Excitation (EOE) is associated with 5-HTTLPR Short/Short Genotype when taking gender, age, psychological distress, and the personality traits Neuroticism, Extraversion, and Openness into account. Partial regression plot of EOE score vs. 5-HTTLPR s/s genotype (s/s = 1, s/l or l/l = 0), (pcorr = 0.23, p = 0.004). Model: adj. $R^2 = 40.4\%$, n = 161. 5-HTTLPR s/s: coeff. = 4.09, se = 1.41.

Conclusions

Sensory Processing Sensitivity was positively correlated with female gender, psychological distress, and the personality traits Neuroticism, Harm Avoidance, and Openness, and negatively correlated with Extraversion.

Higher levels of Sensory Processing Sensitivity were associated with the serotonin transporter 5-HTTLPR short/short genotype, when taking gender, age, psychological distress, and the personality traits Neuroticism, Extraversion, and Openness into account.

In particular, this association was evident for Ease of Excitation, a facet of Sensory Processing Sensitivity.

Neuroticism and Harm Avoidance were not associated with the 5-HTTLPR short/short genotype, or with 5-HTTLPR short allele carrier status.

Thus, the trait Sensory Processing Sensitivity describes a psychological profile associated with homozygous status of a common polymorphism in the serotonin system.

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Acknowledgements

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