

# Serotonin transporter promoter gene polymorphic region (5-HTTLPR) and personality in female patients with seasonal affective disorder and in healthy controls

Nikolaus Thierry<sup>a,\*</sup>, Matthäus Willeit<sup>a</sup>, Nicole Praschak-Rieder<sup>a</sup>, Peter Zill<sup>b</sup>, Kurt Hornik<sup>c</sup>,  
Alexander Neumeister<sup>a</sup>, Elisabeth Lenzinger<sup>a</sup>, Jürgen Stastny<sup>a</sup>, Eva Hilger<sup>a</sup>,  
Anastasios Konstantinidis<sup>a</sup>, Harald Aschauer<sup>a</sup>, Manfred Ackenheil<sup>b</sup>, Brigitta Bondy<sup>b</sup>,  
Siegfried Kasper<sup>a</sup>

<sup>a</sup>Department of General Psychiatry, Waehringer Guertel 18–20, University of Vienna, A-1090 Vienna, Austria

<sup>b</sup>Department of Neurochemistry, Department of Psychiatry, Ludwig Maximilians University, Munich, Germany

<sup>c</sup>Department of Statistics and Probability Theory, University of Technology, Vienna, Austria

Received 8 October 2002; accepted 8 May 2003

## Abstract

Serotonergic pathways have been related to altered personality patterns in seasonal affective disorder (SAD). The short allele (*s*) of a polymorphism in the serotonin transporter promoter gene (5-HTTLPR) has been associated with neuroticism and anxiety-related personality traits in healthy volunteers. We investigated personality and 5-HTTLPR in female SAD patients using the Temperament and Character Inventory (TCI). TCI was completed by 56 female patients and 76 age-matched female controls. DNA was genotyped using polymerase chain reaction methods. Subjects homozygous for the long allele (*l*) were compared to *s* carriers. Females with SAD had higher scores in Harm Avoidance and lower scores in Novelty Seeking, Self-Directedness and Cooperativeness when compared to controls. Patients carrying the *s* allele had lower Self-Directedness scores. Our data indicate that females with SAD show altered personality traits. The *s* allele was associated with lower Self-Directedness scores in SAD patients, whereas there were no significant differences in TCI dimensions between patients and controls in carriers of the long allele.

© 2003 Elsevier B.V./ECNP. All rights reserved.

**Keywords:** 5-HTTLPR; TCI; Seasonal affective disorder; Personality; Serotonin; Depression

## 1. Introduction

Seasonal Affective Disorder (SAD), winter type, is a mood disorder characterized by the regular occurrence of depressive episodes during fall or winter followed by spontaneous remission or hypomanic episodes in spring or summer (Rosenthal et al., 1984). SAD patients fulfill the diagnostic criteria for major depressive disorder or bipolar II disorder, and their longitudinal course is described by the seasonal pattern specifier of the Diagnostic and Statistical Manual 4th Edition (DSM IV, American Psychiatric Association, 1994). Common symptoms in SAD include de-

pressed mood and the so-called atypical or reverse vegetative symptoms such as hypersomnia, hyperphagia, fatigue, carbohydrate craving and subsequent weight gain (Rosenthal et al., 1984). There is strong evidence for a key role of serotonergic systems in the pathogenesis of SAD (Kasper et al., 1996; Lam and Levitan, 2000). Controversy exists of whether serotonergic dysfunction may represent a trait marker in SAD (Schwartz et al., 1997; Neumeister et al., 1998; Lam and Levitan, 2000).

When compared to non-seasonal depressives or controls, SAD has also been reported to be associated with an increased likelihood of personality disorder, reflecting a possible link between personality and seasonal mood changes (Schulz et al., 1988; Schuller et al., 1993; Reichborn-Kjennerud et al., 1994). As proposed by Cloninger et al. (1993), temperament dimensions are believed to repre-

\* Corresponding author. Tel.: +43-1-40400-3544; fax: +43-1-40400-3099.

E-mail address: nikolaus.thierry@akh-wien.ac.at (N. Thierry).

sent biologically based traits, while character traits may rather reflect sociocultural learning processes. This concept was realized in the Temperament and Character Inventory (TCI), a widespread instrument for the assessment of personality disorders (Cloninger, 1994).

The serotonin transporter (5-HTT) is a candidate locus for etiological involvement in affective disorders. A functional polymorphism in the serotonin promoter gene region (5-HTTLPR) has been found to influence serotonin transporter (5-HTT) expression in human cell lines (Heils et al., 1996; Lesch et al., 1996). This polymorphism is a 44-bp insertion/deletion polymorphism located approximately 1 kb upstream from the 5-HTT coding sequence. The short variant (“*s* allele”) of the 5-HTT-linked polymorphic region (5-HTTLPR) restricts transcriptional activity of the 5-HTT promoter, leading to low functional expression of 5-HTT. The HTTLPR short allele (*s*) has been shown to be associated with reduced 5-HTT mRNA levels, lower 5-HTT densities on the cell surface, and reduced 5-HT uptake rates in cultured human lymphocytes (Lesch et al., 1996). The *s* allele appears to be functionally dominant over the 5-HTTLPR long allele (*l*), since heterozygous cells behave like cells homozygous for the *s* allele (Lesch et al., 1996).

It has been reported that the 5-HTTLPR-dependent variation in functional 5-HTT expression may confer a genetic susceptibility towards affective disorders (Collier et al., 1996). Moreover, the *s* allele has been associated with violent suicide behavior (Bondy et al., 2000), alcoholism (Sander et al., 1997), obsessive compulsive disorder (McDougle et al., 1998), and schizophrenia (Malhotra et al., 1998).

Controversy exists as to what extent the 5-HTTLPR polymorphism may contribute to personality dimensions. Several authors reported an effect of the 5-HTTLPR polymorphism on TCI scores such as Harm Avoidance (Cloninger et al., 1993; Allgulander et al., 1997; Peirson et al., 1998; Osher et al., 2000), Novelty Seeking (Benjamin et al., 2000a), Persistence (Benjamin et al., 2000b) and Cooperativeness (Kumakiri et al., 1999). Other studies failed to find an association between 5-HTTLPR polymorphism and personality scores, suggesting that the factor structure of the TCI does not reveal the hypothesized phenotypic structure (Waller et al., 1993; Herbst et al., 2000). There is considerable inconsistency in the association of Neuroticism with 5-HTTLPR from studies using different proportions of male and female subjects. As the effects of 5-HTTLPR are possibly gender related (Du et al., 2000), we conducted our study in females only.

With respect to SAD, Rosenthal et al. (1998) reported an association between the 5-HTTLPR *s* allele with SAD and high levels of seasonality. However, these data were not replicated in more recent studies (Willeit et al., 2003; Johansson et al., 2001). Jang et al. (1997, 1998) found evidence for a hereditary component of seasonal changes in personality measures using the Dimensional Assessment of

Personality Pathology (Livesley and Jackson, 1992) in a sample of homozygotic and heterozygotic twin pairs.

In order to investigate whether 5-HTTLPR polymorphism may contribute to personality dimensions in SAD, we conducted a study on the potential interaction between 5-HTTLPR and personality in SAD patients and healthy controls using the TCI (Cloninger, 1994).

## 2. Experimental procedures

### 2.1. Subjects

Fifty-six female caucasian patients (mean age  $\pm$  S.D.:  $32.9 \pm 9.8$ ) attending our outpatient clinic for SAD were included in the study. Patients were symptomatically depressed (mean SIGH-SAD  $24.6 \pm 5.3$ ), meeting the Rosenthal and DSM-IV criteria for SAD (American Psychiatric Association, 1994; Rosenthal et al., 1984) (see Table 1). Patients with an axis-I diagnosis other than SAD were not enrolled in the study. Controls ( $n = 76$ ; mean age  $32.8 \pm 10.4$ ) were recruited by announcement in the local newspaper. The control group was screened for past and present psychiatric disorders using the Structured Clinical Interview for DSM-IV axis-I disorders (SCID, DSM-IV). Subjects with present or past psychiatric disorders or substance abuse were excluded from the study.

Patients and controls were genotyped for 5-HTTLPR. Personality dimensions were assessed using the German version of the TCI (Richter et al., 1999). All subjects completed the TCI questionnaire during fall (October) and winter (February) 1999/2000. All subjects gave written informed consent after a full explanation of study procedures. The protocol was approved by the Ethics Committee of the University of Vienna.

### 2.2. Genotyping

Genotyping was performed using peripheral nuclear cells obtained by centrifugation of approximately 5 ml blood from the antecubital vein. 5-HTTLPR genotypes were

Table 1  
Clinical and demographic characteristics of patients and controls

	SAD ( $n = 56$ )	CON ( $n = 76$ )	
Age $\pm$ S.D.	$32.9 \pm 9.8$	$32.8 \pm 10.4$	$P = \text{n.s.}^*$
GSS	$16.5 \pm 4.1$	$2.9 \pm 2.1$	$P < 0.001^*$
<i>Subtype (DSM IV)</i>			
Atypical subtype	47 (83.9%)	–	–
Melancholic subtype	9 (16.1%)	–	–
Positive FH	32 (57.1%)	19 (25%)	$P < 0.001^*$

SAD, seasonal affective disorder; CON, healthy controls; GSS, global seasonality score; DSM IV, Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; FH, family history for DSM IV psychiatric disorder; \*two-tailed *t*-test.

متن کامل مقاله

دریافت فوری ←

**ISI**Articles

مرجع مقالات تخصصی ایران

- ✓ امکان دانلود نسخه تمام متن مقالات انگلیسی
- ✓ امکان دانلود نسخه ترجمه شده مقالات
- ✓ پذیرش سفارش ترجمه تخصصی
- ✓ امکان جستجو در آرشیو جامعی از صدها موضوع و هزاران مقاله
- ✓ امکان دانلود رایگان ۲ صفحه اول هر مقاله
- ✓ امکان پرداخت اینترنتی با کلیه کارت های عضو شتاب
- ✓ دانلود فوری مقاله پس از پرداخت آنلاین
- ✓ پشتیبانی کامل خرید با بهره مندی از سیستم هوشمند رهگیری سفارشات