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Research report

The 5HTTLPR polymorphism of the serotonin transporter gene is associated with affective temperaments as measured by TEMPS-A

Xenia Gonda [a,b], Zoltan Rihmer [b], Terezia Zsombok [a], Gyorgy Bagdy [a,c,*], Kareen K. Akiskal [d,e], Hagop S. Akiskal [d,e,f,g]

[a] *Laboratory of Neurochemistry and Experimental Medicine, National Institute for Psychiatry and Neurology, Budapest, Hungary*
[b] *National Institute for Psychiatry and Neurology, Psychiatry No. III, Budapest, Hungary*
[c] *Group of Neuropsychopharmacology, Hungarian Academy of Sciences and Semmelweis University, Budapest, Hungary*
[d] *International Mood Center, La Jolla, California, USA*
[e] *Union of Depressive and Manic–depressive Association, Rennes, France*
[f] *Department of Psychiatry, University of California at San Diego, La Jolla, California, USA*
[g] *Veterans Administration Medical Center, San Diego, California, USA*

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Abstract

Background: Increasing evidence supports the notion of a continuum between affective temperaments and major mood disorders, suggesting that these temperament types represent the subclinical manifestations of affective disorders and often present an increased vulnerability for these diseases.
Methods: The Hungarian rendition of the full-scale 110-item version of the TEMPS-A questionnaire and 5HTTLPR genotype was investigated in a sample of 139 unrelated Caucasian females with no current or lifetime Axis I psychiatric disorders.
Results: A significant association was found between the s allele and the TEMPS scores of the depressive, anxious, irritable, and particularly the cyclothymic temperaments; no such association emerged with respect to the hyperthymic temperament.
Limitation: The database is entirely female. Given that the hyperthymic type predominates in males, our results could have been different if men were included in our sample.
Conclusions: Our results are in good agreement with earlier studies reporting a strong association between the s allele of the 5HTTLPR and major as well as subthreshold forms of depression, and extend this association to the normative temperament level. Indeed, these temperaments might best be regarded as proximate behavioural endophenotypes. Our data raise the provocative possibility that the genetic potential for mood episodes lies in these temperaments. Further studies are needed to delineate the role of gender in the associations under consideration, as well as to investigate the genetic background of the hyperthymia–mania part of the affective spectrum. Given that affective temperaments are widely distributed in the general population, the strategy employed by us is of potential public health significance in terms of detecting individuals in the community at risk for affective spectrum disorders.

Keywords: Depression; Serotonin transporter; Affective temperaments; TEMPS-A; Endophenotype; Genetics

* Corresponding author. National Institute for Psychiatry and Neurology, Laboratory of Neurochemistry and Experimental Medicine, 1021 Budapest, Huvosvolgyi ut 116. Tel.: +36 1 391 5407; fax: +36 1 391 5408.
E-mail address: bag13638@mail.iif.hu (G. Bagdy).

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1. Introduction

In support of the clinical view of Kraepelin (1921) and Kretschmer (1936), recent clinical follow-up investigations as well as familial–genetic, biological, and treatment–response studies have demonstrated that there is a continuum between Cyclothymia–Bipolar II–Bipolar I disorder (Akiskal et al., 1977; Akiskal et al., 1995; Kochman et al., 2005), and the same is true for the subsyndromal depression–minor depression/dysthymia–unipolar major depression spectrum (Akiskal et al., 1978; Akiskal et al., 1980; Rihmer et al., 1983; Rihmer and Szádóczky, 1993; Rihmer, 1990, 1999; Judd and Akiskal, 2000; Lewinsohn et al., 2003). The results also suggest that the specific different affective temperament-types (hyperthymic, cyclothymic, depressive, irritable, anxious) are the subaffective/embrional (trait-related) manifestations and frequently the precursors of the major depressive and bipolar and unipolar mood disorders (Akiskal and Akiskal, 1992; Akiskal, 1995, 1996; Akiskal and Pinto, 1999; Kochman et al., 2005).

There is plausible evidence that central serotonergic function is dysregulated in a substantial part of patients with unipolar and bipolar major depressive episode (Goodwin and Jamison, 1990; Den Boer et al., 2001), and recently a significant association between the s allele of the serotonin transporter gene and unipolar and bipolar major depression has been also reported by some (Bellivier et al., 1998; Hauser et al., 2003; Caspi et al., 2003; Lotrich and Pollock, 2004), but not all (Willis-Owen et al., 2005) authors.

Most recently, we found a significant connection between the s allele of the serotonin transporter gene and subthreshold depressive symptoms in 128 females without any lifetime DSM-IV Axis I diagnoses (Gonda et al., 2005), providing support of a subthreshold–minor–major depression continuum (Akiskal, 1994; Judd and Akiskal, 2000; Rihmer, 1990) from a molecular genetic point of view.

Considering the familial (possibly genetic) basis for the hyperthymic and cyclothymic temperaments in the genesis of bipolar disorder (Kraepelin, 1921; Chiaroni et al., 2005; Evans et al., 2005; Kesebir et al., 2005), and postulating the same for the unipolar depressive spectrum (Akiskal, 1994), the aim of our present study was to examine whether the genetic vulnerability for depression, as reflected in the serotonin transporter gene 5HTTLPR polymorphism, could be retraced through the major–minor–subthreshold continuum of depression all the way to the temperamental level.

2. Method

2.1. Subjects

139 unrelated females of Caucasian origin participated in the study. The age of the participants was 18–62 years, the mean age was 31.39±1.0279 years. All subjects went through thorough neurological and psychiatric screening. Subjects with any neurological and current or lifetime Axis I psychiatric disorders according to the DSM-IV (American Psychiatric Association, 1994) criteria were excluded. The study protocol was approved by the local ethics committee for experimentation on humans and every subject gave informed consent before participating in the study. All subjects completed the Hungarian version (Rózsa et al., in press) of the original, 110-item TEMPS-A questionnaire (Akiskal and Akiskal, 2005) and were genotyped for the 5HTTLPR polymorphism.

2.2. Genotyping

Polymerase chain reaction (PCR) amplification of 5HTTLPR was performed on genomic DNA extracted from white blood cells. The 5HTTLPR genotypes were identified as previously reported (Heils et al., 1996; Juhasz et al., 2003a,b). Primers for 5HTTLPR were 5′-GGCGTTGCCGCTCTGAATGC-3′(STPR5) and 5′-GAGGGACTGAGCTGGACAACCAC-3′ (STPR3).

Table 1
Analysis of variance table for the TEMPS-A subscale scores of subjects carrying the s allele and subjects not carrying the s allele

	SS effect	*df* effect	MS effect	SS error	*df* error	MS error	*F*	*p*
Depressive	37.9482	1	37.9482	1305.879	137	9.53196	3.981157	0.0480*
Cyclothymic	72.8207	1	72.8207	2073.784	137	15.13711	4.810742	0.0299*
Hyperthymic	5.3081	1	5.3081	2202.519	137	16.07678	0.330172	0.5665
Irritable	46.3714	1	46.3714	1586.578	137	11.58086	4.004139	0.0474*
Anxious	103.5899	1	103.5899	3583.115	137	26.15413	3.96074	0.0486*

Significant effects are denoted by *.