

Behavioral effects of tryptophan depletion in seasonal affective disorder associated with the serotonin transporter gene?

Elisabeth Lenzinger^{a,*}, Alexander Neumeister^a,
Nicole Praschak-Rieder^a, Karoline Fuchs^b, Elisabeth Gerhard^b,
Mattheus Willeit^a, Werner Sieghart^b, Siegfried F. Kasper^a,
Kurt Hornik^c, Harald N. Aschauer^a

^aDepartment of General Psychiatry, University Hospital for Psychiatry, Vienna, Austria

^bDivision of Biochemical Psychiatry, University Hospital for Psychiatry, Vienna, Austria

^cInstitut für Statistik und Wahrscheinlichkeitstheorie, Technische Universität Wien, Vienna, Austria

Received 28 July 1998; received in revised form 8 December 1998; accepted 29 December 1998

Abstract

There is some evidence that the neurotransmitter serotonin (5-hydroxytryptamine; 5-HT) may be involved in the pathogenesis of seasonal affective disorder (SAD). Short-term tryptophan (TRP) depletion was carried out in 18 drug-free remitted patients who met DSM-IV criteria for SAD. Behavioral effects were measured with the Hamilton Depression Rating Scale (HDRS) both 24 h before and 24 h after TRP depletion. Some of the patients showed behavioral responses such as lowered mood, feelings of guilt, loss of interest, agitation, loss of energy, fatigue, social withdrawal, increased appetite, and carbohydrate craving. It was the aim of our study to investigate whether the genotypes of the serotonin transporter gene were associated with symptoms of transient depressive relapse after TRP depletion. In addition, we matched the SAD patients with healthy control subjects to see if alleles and genotypes of the serotonin transporter gene were associated with SAD. High molecular weight DNA was isolated from peripheral blood leukocytes using standard methods. For the 5-HTT receptor gene, a 17-bp repetitive element of intron 2 was genotyped (variable number tandem repeat, VNTR). Alterations in HDRS scores after TRP depletion showed no significant association with alleles or genotypes of the 5-HTT gene, although heterozygotes showed a trend toward increased HDRS scores. The serotonin transporter is known to play a critical role in the termination of serotonergic

* Corresponding author. Tel.: +43 1 404003543; fax: +43 1 404003099.

neurotransmission by sodium-dependent uptake of 5-HT into the presynaptic neuron. The present study in a small group of SAD patients was unable to demonstrate that the 5-HTT gene plays a role in the pathogenesis of SAD or in short-term depressive relapse after TRP depletion. © 1999 Elsevier Science Ireland Ltd. All rights reserved.

Keywords: Depressive disorder; Chronobiology; Variable number tandem repeat polymorphism; Genetics

1. Introduction

Although seasonal patterns in the occurrence of depression have long been recognized (cf. Wehr and Rosenthal, 1989), only in recent years have the syndromes of recurrent seasonal depression been described more precisely (Rosenthal et al., 1984; Wehr et al., 1987; Kasper et al., 1989). Seasonal affective disorder (SAD) is not only characterized by annual recurrences of depressive episodes in fall and winter months, with spontaneous remissions in spring and summer, but also by the predominance of atypical symptoms like fatigue, social withdrawal, increased appetite and carbohydrate craving (Kasper et al., 1988a,b). Some of the neurovegetative functions that are disturbed in SAD are related to the serotonin (5-hydroxytryptamine; 5-HT) system — for example, the regulation of appetite and weight (Rosenthal et al., 1987). The high carbohydrate intake of SAD patients during fall and winter could represent a behavioral–biochemical feedback loop for raising the available 5-HT content (Fernstrom, 1977), which may explain why patients with SAD frequently report activation after carbohydrate ingestion. Evidence for a seasonal rhythm of human hypothalamic 5-HT has been reported (Carlsson et al., 1980; Klompenhouwer et al., 1990). Moreover, Brewerton et al. (1988) demonstrated that the levels of the serotonin metabolite 5-hydroxyindoleacetic acid (5-HIAA) in cerebrospinal fluid are much higher in summer and fall than in winter and spring. Thus, it is possible that in the pathogenesis of SAD this physiological variation could represent a pathological variant.

Serotonergic medications appear to be effective in the treatment of SAD (Ruhmann et al., 1993; Lam et al., 1996). The antidepressant effect of light therapy may also be mediated through serotonergic mechanisms because tryptophan (TRP)

depletion reverses the anti-depressant effect of bright light therapy and causes a lowering of mood in drug-free remitted SAD patients (Lam et al., 1996).

The serotonin transporter plays a critical role in the termination of serotonergic neurotransmission by sodium-dependent uptake of 5-HT into the presynaptic neuron (Lesch et al., 1994). A single gene encodes the human serotonin transporter, which has been mapped to chromosome 17q11.2. A polymorphism of its intron 2 containing a variable number tandem repeat (VNTR) region has been identified (Lesch et al., 1994).

The dimensions of SAD range from mild to severe signs and symptoms, and TRP depletion may cause a reversible relapse in remitted patients that is of the same magnitude as the clinical depression. Behavioral and biochemical effects of TRP depletion in the group of SAD patients described here have been previously reported (Neumeister et al., 1997). The present report examined whether the serotonin transporter gene (5-HTT) was: (1) involved in the pathogenesis of SAD; and (2) related to the severity of the behavioral effects after TRP depletion.

2. Methods

2.1. Subjects

Eighteen drug-free outpatients (16 females, two males; mean age = 41.89 years, range = 27–70 years) from our SAD clinic agreed to participate in a study on the behavioral effects of short-term TRP depletion. All patients were diagnosed as meeting DSM-IV criteria (American Psychiatric Association, 1994) for SAD by consensus of clinic psychiatrists. Apart from the diagnosis of SAD, all patients were free of medical and neurological

متن کامل مقاله

دریافت فوری ←

ISIArticles

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