



PERGAMON

Available online at www.sciencedirect.com

SCIENCE @ DIRECT®

Journal of Psychiatric Research 37 (2003) 229–235

JOURNAL OF
PSYCHIATRIC
RESEARCH

www.elsevier.com/locate/jpsychires

Plasma levels of soluble transferrin receptors and Clara cell protein (CC16) during bipolar mania and subsequent remission

Shang-Ying Tsai^{a,b,*}, Hsin-Chien Lee^b, Chiao-Chicy Chen^{a,c}, Chao-Hsien Lee^d

^aDepartment of Psychiatry, School of Medicine, Taipei Medical University, Taipei, Taiwan

^bDepartment of Psychiatry, Taipei Medical University Hospital, Taipei, Taiwan

^cDepartment of Adult Psychiatry, Taipei City Psychiatric Center, Taipei, Taiwan

^dGraduate Institute of Epidemiology, College of Public Health, National Taiwan University, Taiwan

Received 9 September 2002; received in revised form 12 November 2002; accepted 12 December 2002

Abstract

Clara cell protein (CC16) and transferrin receptor (TfR) have been reported as possible biological markers for major depression and schizophrenia. However, the alternations of plasma TfR and CC16 levels and the influences of numerous clinical variables on them during bipolar mania are not sufficiently described. We investigated the immune function of 36 bipolar I, manic (DSM-IV) patients with Young Mania Rating Scale (YMRS) scores ≥ 26 as well as during the subsequent remission (YMRS ≤ 12) and age- and sex- matched healthy controls. The plasma TfR levels were increased during acute mania along with subsequent remission and were independent of medication status, individual variations, clinical and erythrocyte variables. Among inflammatory parameters and haematological variables, the plasma TfR levels merely had significant and negative relationship with the percentage of monocyte in circulating leukocyte counts despite of elevated plasma soluble interleukin-2 receptors levels during bipolar mania. The plasma levels of CC16 of bipolar patients did not significantly alter during acute mania, whereas smoking, body mass index, and co-existing psychotic features collectively contributed 42% of the plasma levels of CC16. We provide additional evidence to indicate the pathophysiological role of the immune systems in affective disorders. It is suggested that the elevation of plasma TfR levels might be a trait phenomenon in bipolar disorder.

© 2003 Elsevier Science Ltd. All rights reserved.

Keywords: Clara cell protein (CC16); Transferrin receptor (TfR); Bipolar mania in Taiwan; Immune-inflammatory parameter; Erythrocyte; Monocyte; Biological marker

1. Introduction

There is increasing evidence that bipolar mania is characterized by the activation of the inflammatory response system (IRS) with increasing serum concentration of positive acute phase proteins (Hornig et al., 1998), increased plasma soluble interleukin-2 receptor (sIL-2R) levels (Maes et al., 1995a; Tsai et al., 1999; 2001), and elevated mitogen-induced lymphocyte proliferation (Tsai et al., 1999).

It has been suggested that the affective disorders and schizophrenia are accompanied by *in vivo* activation of cell-mediated immunity as indicated by higher plasma

levels of sIL-2R and transferrin receptor (TfR) (Connor et al., 1998; Maes et al., 1995a; 1995c). Expression of the TfR, a transmembrane glycoprotein, is regulated by two distinct mechanisms: the growth rate of cells and their requirements for iron (Woith et al., 1993). The TfRs are expressed at the cell surface of normal proliferating cells and are shed off into the plasma to act as a necessary signal promoting lymphocyte proliferation (de Jong et al., 1990; Keyna et al., 1991). Moreover, the plasma TfR level is an excellent marker for erythropoiesis (Huebers et al., 1990) and may be a promising tool to detect iron deficiency during inflammatory states (Feelders et al., 1999). Physiological changes in serum TfR are related not only to small alternations in the iron supply to the erythroblasts, storage iron, erythrocyte haemoglobinization, and erythropoiesis, but also to changes in the immune status such as T-cell activation

* Corresponding author. Tel.: +886-2-22344850; fax: +886-2-27372189.

E-mail address: tmcpsyts@tmu.edu.tw (S.-Y. Tsai).

(Maes et al., 1997a). Increased plasma TfR level has been considered as a trait marker of major depression (Maes et al., 1995b). To our knowledge, only a 10-patient study demonstrated higher plasma TfR levels during bipolar mania (Maes et al., 1995a). However, confounding effects of numerous clinical or individual factors on plasma TfR levels in bipolar patients remain unclear.

Clara cell protein (CC16) is secreted by Clara cells in the lining fluid of bronchiolar and bronchial epithelium. The CC16 may have immunosuppressive and anti-inflammatory properties (Hermans and Bernard, 1996). Lowered serum CC16 may be a trait marker of schizophrenia and is likely related to the increased serum sIL-6R (Maes et al., 1996). Increasing serum CC16 concentrations in euthymic patients undergoing lithium treatments was reported (Rybakowski, 2000), but our early works found that there is no alternation of plasma sIL-6R levels during bipolar mania (Tsai et al., 1999; 2001). Unfortunately, no further report was available regarding serum CC16 levels in patients with bipolar disorder to illustrate the different immunomodulatory mechanism in various psychiatric conditions.

It is difficult to determine whether immune-inflammatory parameters play a role in the pathophysiology of psychiatric disorders before carefully taking into account confounding factors, such as influence of medication (Pollmächer et al., 2000; Rapaport and Manji, 2001), body mass index (BMI), and a variety of clinical variables (Haack et al., 1999). Thus, it is hypothesized that the plasma levels of CC16 or TfR may alter during acute mania and may be affected by medication, smoking, individual variation, or other psychopathological characteristics. Studies investigating the cytokines and soluble cytokine receptors should include simultaneous complete blood counts and employ more measures of clinical status to correlate with immune measures (Rapaport et al., 1999). Therefore, our goals were first to investigate the changes of plasma CC16 and TfR levels during acute mania in a large sample of bipolar disorder and to analyze the effects of medication and clinical characteristics on their levels. We also wanted to determine the relationship between plasma TfR levels and immune-inflammatory parameters (sIL-2R and sIL-6R) as well as haematological variables of bipolar manic patients.

2. Methods

2.1. Patients

The sample presented was independent from our prior works (Tsai et al., 1999; 2001) and an appropriate ethical committee approved the study protocol. Patients of the Department of Psychiatry of Taipei Medical Uni-

versity Hospital and the Taipei City Psychiatric Center in Taiwan who met the DSM-IV criteria for bipolar I disorder were recruited. These patients were interviewed by two experienced psychiatrists with a well-validated semi-structural schedule in Chinese, the Psychiatrist Diagnosis Assessment, which has been successfully used and extensively described elsewhere (Tsai et al., 1997; 1999). The severity of affective symptoms was rated on the Young Mania Rating Scale (YMRS) (Young et al., 1978) and 24-item Hamilton Depression Rating Scale (HDRS) (Hamilton, 1960). Based on the criteria of DSM-IV, diagnoses were made in consensus meetings. Bipolar I patients with YMRS scores ≥ 26 , and aged 16–45 years were eligible for participation in this study. Patients with current mixed episode, comorbid substance use disorders, symptoms of allergies, chronic or acute infection, history of autoimmune diseases, or any other conditions known to affect the immune system for at least 2 weeks before the study were excluded. The patients were treated with lithium or valproate, and typical antipsychotics (mainly haloperidol) were given when clinically indicated.

2.2. Healthy control

Age- and gender-matched normal volunteers without any medical illness participated in the study as the healthy controls. None of these subjects regularly consumed alcohol/substance or had taken drugs known to alter immune or endocrine function for at least 2 weeks prior to the study. All healthy controls were screened for present and past history of any DSM-IV axis I disorder by means of a well-validated Chinese version of the General Health Questionnaire (Cheng & Williams, 1986) followed by a semi-structured interview performed by experienced psychiatrists.

After written informed consent was obtained, all patient and healthy controls were screened for abnormalities by physical examination, complete blood counts with differentials, serum enzyme and metabolite screening, urine analysis and thyroid function tests.

2.3. Clinical variables

Data on clinical features were sought by means of direct interview with the patients and other individuals considered to have reliable information and by a review of medical records, including continuous variables (age, age at onset, number of prior affective episodes, duration of affective syndrome and psychotropic medication before blood sampling, lithium dosage, valproate dosage, CPZ equivalents [mg chlorpromazine/day], BMI, and YMRS scores); and categorical variables (sex, past history of major depression, smoking, family history of mood disorder in first-degree relatives, and co-existing psychotic features [delusions or hallucinations]).

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