

Psychopathological and nutritional correlates of plasma homovanillic acid in adolescents with anorexia nervosa

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Received 2 May 2006; received in revised form 11 October 2006; accepted 23 October 2006

Abstract

Dopaminergic abnormalities have been described in anorexia nervosa but studies about plasma level of homovanillic acid (pHVA) have yielded conflicting results probably due to the small number and the heterogeneity of patients. Plasma HVA, nutritional and hormonal parameters and several scales – the Eating Attitudes Test (EAT), the Beck Depression Inventory (BDI), the Leyton Obsessional Inventory-child version (LOI-C) and the State and Trait Anxiety Inventory (STAI) – were assessed in 44 adolescent anorexia nervosa patients (mean age 14.7 years, SD 1.7) consecutively admitted to an Eating Disorder Unit. They were evaluated at admission, at discharge and, in 34 cases, after 9 months of follow-up. pHVA was also assessed in 16 control adolescents. Patients had significantly higher pHVA than controls ($p = .002$). About 31% of patients had a very high level of pHVA, a significantly higher ($p = .006$) mean score in the BDI and a non significantly higher mean score in the EAT. After weight recovery some laboratory parameters improved as well as the EAT ($p = .019$), the BDI ($p = .001$) and the Interference score of the LOI-C ($p = .004$). Moreover, pHVA decreased significantly ($p = .036$). At follow-up, patients with normal weight had lower ($p = .037$) pHVA than patients with low weight. The conclusion would be that there is a dopaminergic dysfunction in anorexic patients, specially in a subgroup with high depressive and anorexic symptomatology. With weight recovery and psychopathological improvement, pHVA tends to normalization.

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Keywords: Anorexia nervosa; Adolescents; Homovanillic acid; pHVA; Dopamine; Weight recovery

1. Introduction

Anorexia nervosa is a disorder that tend to begin in adolescence and has severe physical morbidity and psychosocial disability as well as the highest mortality of any psychiatric disorder (Harris and Barraclough, 1998; Sullivan, 1995). Dopaminergic abnormalities have been related to altered feeding behavior and it has been suggested that they can be involved in the symptomatology of anorexia

nervosa (Barry and Klawans, 1976). Studies with rats show that a dopaminergic deficit leads to a decrease of eating and drinking behavior (Johansen et al., 2001; Zhou and Palmiter, 1995) while restoration of dopamine production within the caudate putamen restores feeding (Szczyepka et al., 2001). Nevertheless, very high dopaminergic stimulation may suppress feeding in rats (Yang et al., 1997). In humans, a higher food intake restraint has been related to greater dopaminergic responsivity to food stimuli (Volkow et al., 2003). These conflicting results may indicate that there is an optimal level of dopaminergic activity to mediate an adequate feeding and that both high and low

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dopamine levels may interfere with it. Golden and Shenker (1994) described a significantly impaired prolactin response to metoclopramide, a central D-2 dopamine receptor blocker, in 10 women with anorexia nervosa. Brambilla et al. (2001) found growth hormone responses to apomorphine stimulation significantly lower in 16 restrictive and purgative anorexic patients than in controls subjects, suggesting a subsensitivity of postsynaptic D-2 receptors and possible a presynaptic dopaminergic hypersecretion. Besides that, recovered anorexia nervosa patients have higher [^{11}C] raclopride binding potential in the antero-ventral striatum than control subjects and an increased D2/D3 receptor density or a decreased intrasynaptic dopamine concentration have been suggested (Frank et al., 2005). Moreover, another study has found that anorexia nervosa patients have altered frequency of a functional polymorphism for D2 receptor genes suggesting that affected receptor transcription and translation efficiency may play a role in vulnerability to anorexia nervosa (Bergen et al., 2005). Barbato et al. (2006) found that eye blink rate, a peripheral measure of central dopaminergic activity, was significantly increased in anorexic patients. All these results suggest an important role for altered dopaminergic activity in anorexia nervosa patients.

Homovanillic acid concentration, a dopamine metabolite, in cerebrospinal fluid or in plasma, has been considered a measure of central dopaminergic activity and its significance comes from some studies that have found that plasma HVA predicts severity of symptoms (Breier et al., 1993; Zhang et al., 2001) and response to antipsychotic treatment (Chang et al., 1990; Yoshimura et al., 2003) in psychotic patients reflecting a relationship between plasma HVA and central processes. Results from earlier studies of homovanillic acid in patients with anorexia nervosa have found a diminished level of this metabolite. Kaye et al. (1984) found a 30% decrease of cerebrospinal fluid HVA in underweight anorexic patients and Gerner et al. (1984) found that HVA levels were positively related to body weight in anorexic patients. Other small study did not find differences in urinary excretion of HVA between control subjects and six anorexia nervosa patients (Johnston et al., 1984). Nevertheless, more recent studies with larger number of patients, have found higher plasma HVA in eating disorder patients and psychoses in comparison with other psychiatric patients (Bowers et al., 1994, 1988). Conflicting results in different studies can be due to the small number of patients included in many of them, being then difficult to differentiate subgroups of patients, and the heterogeneity of patients included (i.e. different moments of the disorder in which data are collected, duration of disorder or age).

The main objective of the present study was to determine the psychopathological and nutritional variables related to pHVA level in underweight adolescents with short duration anorexia nervosa. The second objective would be to study the changes in this metabolite after short-term weight recovery and after 9 months follow-up considering also patients different outcome.

2. Methods and materials

2.1. Subjects

Forty-four children and adolescents aged 10–17 years who fulfilled the DSM-IV diagnostic criteria (American Psychiatric Association, 1994) for anorexia nervosa were studied. All patients were consecutively admitted to the Eating Disorders Unit of the Child and Adolescent Psychiatry and Psychology Department of the Hospital Clínic Universitari (Barcelona, Spain) and entered in a longitudinal prospective study. All cases of eating disorder not otherwise specified were not included to maintain homogeneity. Clinical characteristics were recorded and laboratory data including pHVA were collected and several scales administered at admission and at discharge. A third complete evaluation was carried out in 34 patients after 9 months follow-up. This third evaluation was not performed in 10 patients who were transferred to other treatment settings. Plasma HVA was also determined in 16 control adolescents (9 males and 7 females) of similar age from the general population.

Parents and subjects were told the purpose of the study and written informed consent was obtained from parents to participate. Study procedures were approved by the Ethics Committee of the Institution.

2.2. Treatment program

All patients followed the usual treatment program in the Unit. This treatment is based on a multidisciplinary approach that combines biological management, nutritional rehabilitation, a behavioral program aimed at improving eating patterns and weight, individual and group cognitive treatment, and individual and group parent counseling. After partial weight recovery, psychopharmacological treatment with selective serotonin reuptake inhibitors (SSRI) is also administered to patients with noticeable depressive or obsessive symptoms even if they did not fulfill diagnostic criteria for depression or obsessive-compulsive disorder. During hospitalization all patients received a complete diet of about 1250 calories per day during the first days which is increased progressively to 2500 calories per day, but they did not receive vitamin supplements or any hormonal replacement therapy. The minimum weight increase per week required during hospitalization is 900 g, which is achieved through a behavioral treatment program. Provided they reach this minimum, patients can decide freely the amount of food intake and, if they prefer, they can try to achieve a somewhat higher rate of weight gain. During the admission treatment program patients achieve normal body mass index for age and sex. Criteria for discharge are weight recovery and normalization of eating patterns. After discharge patients need long-term psychological follow-up on an outpatient basis because the psychological improvement during a short inpatient stay is insufficient.

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