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Decreased platelet monoamine oxidase activity in female bulimia nervosa

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Abstract

The involvement of brain serotonin systems in the pathophysiology of eating disorders has been repeatedly demonstrated in recent studies. Platelet MAO activity is an index of brain serotonin activity and lowered platelet MAO levels have been found in association with impulsive behaviors. In addition, some preliminary reports indicate that platelet MAO could be lowered in eating disorder patients. *Methods:* 47 patients with DSM-IV eating disorders were studied, including 30 with bulimia nervosa and 17 with anorexia nervosa binge eating–purging type. Platelet MAO activity was measured by isotopic methods using C-14 benzylamine and compared with a control group of 30 healthy subjects. Impulsive personality features were studied with specific rating scales. *Results:* Platelet MAO activity was significantly lower (4.4 ± 2.4 nmol/h/10^8 platelets) in the bulimic patients than in the control group (6.9 ± 2.5) ($p<0.001$). No significant differences were found between pure bulimics and binge eating–purging anorectics. Platelet MAO was inversely and significantly correlated with scores on impulsivity scales and with borderline personality disorder characteristics. *Conclusions:* Platelet MAO activity is lowered in patients with bulimia, which may reflect dysfunction in impulse control mechanisms. Since platelet MAO has a predominant genetic component, there is need for studies on the association of low platelet MAO and higher risk for developing eating disorders.

Keywords: Bulimia nervosa; Platelet monoamineoxidase (MAO); Serotonin; Psychobiology; Personality; Impulsivity

1. Introduction

Despite considerable evidence suggesting a link between serotonin (5-HT) function and eating disorders, studies on the functional activity of serotonin are inconclusive. Studies on 5-HT transmission in anorexia nervosa have yielded contradictory results. While some reports have found increased levels of plasma 5-HT and of spinal 5-HIAA in anorectic patients (Kaye et al., 1991), reports on lowered 5-HT function in anorexia nervosa are also described (Hassanyeh and Marshall, 1991). In this sense blunted prolactin concentrations after *m*-cpp and tryptophan administration have been found (Brewerton et al., 1990; Monteleone et al., 1998) suggesting a decreased serotonin receptor sensitivity in anorexia nervosa.

Most studies have described decreased 5-HT function in patients with bulimia nervosa (Smith et al., 1999). Baseline concentrations of prolactin are lowered in bulimic patients and the response of prolactin has been consistently described as blunted after administration of tryptophan, *m*-cpp, and fenfluramine (Brewerton et al., 1992; Goldbloom et al., 1996; Kaye et al., 1998; Monteleone et al., 1998)

Platelet monoamine oxidase activity (MAO) has been proposed as an index of cerebral 5-HT activity (Oreland and Shaskan, 1983) and has been studied in relation with various psychiatric disorders. Lowered platelet MAO has been repeatedly found in patients with impulsive features, including violent offenders (Alm et al., 1994; Castrogiovanni et al., 1994), impulsive drug users (Von

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Knorring and Oreland, 1985), pathological gamblers (Moreno et al., 1991; Carrasco et al., 1994) and borderline personality disorder (Verkes et al., 1996). Preliminary reports indicate that impulsive bulimia could be associated with lowered platelet MAO (Hallman et al., 1990; Verkes et al., 1996). Low platelet MAO in bulimic patients has been interpreted as a confirmation of decreased 5-HT turnover in these patients. However, the above mentioned studies are inconclusive, due to the small samples of patients and the lack of uniformity of diagnostic criteria of anorexia and bulimia used in the different studies (Biederman et al., 1984).

To confirm these results, a study of platelet MAO activity was designed in a sample of 47 patients with impulsive bulimia, strictly delimited according to DSM-IV diagnostic criteria and including those with bulimia nervosa and those with bulimia associated to anorexia nervosa.

2. Methods and materials

Forty seven patients with DSM-IV eating disorders (mean age±S.D.: 21.53±4.2 years) and 30 healthy controls (mean age±S.D.: 23±1 years) were studied. Patients were consecutively included in the study at admission in the outpatient clinic of the Ramón y Cajal hospital. Eating disorders were classified according to DSM-IV diagnostic criteria, resulting in 30 patients with bulimia nervosa and 17 with anorexia nervosa binge eating–purging type. All the patients were drug free for one month before the study. Patients with current major depressive episodes were excluded as well as patients with lifetime bipolar disorder, psychotic disorders or history of alcoholism or substance abuse disorders. Since platelet MAO concentrations vary among sexes, only female patients and female controls were included in the study.

2.1. Psychological measurements

All subjects underwent a psychopathological assessment with the Eating Disorders Inventory (EDI) (Garner et al., 1983) and the Bulimic Investigation Test Edinburgh (BITE) (Henderson and Freeman, 1987) to quantify the symptoms of abnormal eating behavior. Concomitant depression and anxiety were rated with the Hamilton Anxiety and Depression scales. Impulsive features were evaluated with the Barrat's Impulsiveness Scale (Barrat, 1972), a self-control scale (Rosembaum, 1980) and with analogue visual scales specifically designed.

The structured Interview for Personality Disorders (SCID-II) was administered to patients and controls for diagnosis of comorbid personality disorders and for quantitative measurement of specific features of each personality condition.

2.2. Biological studies – Measurement of platelet MAO activity

Participants were asked to refrain from taking coffee or other stimulating beverages the night before the study. Blood samplings were collected at 9:00 h, after a 12 h fast and after a one night sleep of at least 7 h duration. Thirty ml of blood were obtained by antecubital venipuncture and were collected in tubes containing 0.129 M trisodium citrate as anticoagulant (Vacutainer). The samples were immediately processed by centrifugation for 15 min, obtaining platelet-rich plasma (PRP) free from red and white blood cells. The concentration of platelets in PRP was measured by electronic count (Coulter Thrombocounter).The measurements of platelet MAO were made immediately after sampling, following the basic technique of (Murphy et al. (1976).

PRP was transferred to test tubes containing 0.1 ml of potassium phosphate buffer (1.0 mol/l, pH 7.4). Every duplicate tube also contained 0.1 ml of pargyline (2.4 mmol/l, in 1 mmol/l HCl).

After preincubation at 37°C for 10 min, 100 micromol of 14C-benzylamine (4.0 mmol/l, 600 microCi/mmol, Amersham International) was added and incubated for 30 min at 37°. The reaction was stopped by the addition of 0.3 ml of 3 M Hcl in each tube. The reaction products were recovered with heptane, centrifuged and added to 10 ml of scintillation liquid for radioactivity determination. C-14 activity was expressed as disintegrations per min per ml of reaction product. Isotopic counting due to MAO activity was calculated as the difference between the tubes with and without pargyline. Platelet MAO activity is reported as nmol of product per hour per 10^8 platelets.

Both inter and intra-assay coefficients were less than 10%. Measurements were made simultaneously in patients and controls, intercalating individuals from both groups to avoid biases due to variations in environmental conditions.

2.3. Statistical analysis

Differences in MAO activity and on the psychological variables between patients and controls were calculated by two-tailed Mann-Whithney U test for nonparametric variables.

ANOVA and two-tailed *t*-tests were used to evaluate the differences of platelet MAO between patients and controls. ANCOVA of platelet MAO was also used to evaluate the influence of other variables such as tobacco smoking and menstrual cycle on platelet MAO variance.

Linear correlations were used for analysis of relationships of biological and psychological variables, with two-tailed significance at $p<0.05$.