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Antioxidant enzyme and malondialdehyde levels in patients with social phobia

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Abstract

A growing body of reports have indicated that free radicals are involved in the etiopathogenesis of some neuropsychiatric disorders. In the present study, we aimed to evaluate whether antioxidant enzymes (superoxide dismutase; SOD, glutathione peroxidase; GSH-Px, and catalase; CAT) activity levels and malondialdehyde (MDA), a product of lipid peroxidation, were associated with social phobia (SP). Eighteen patients diagnosed with SP and 18 healthy controls were enrolled. A clinical evaluation and measurements of MDA, SOD, GSH-Px and CAT were performed. Additionally, all patients were assessed with the Liebowitz Social Anxiety Scale (LSAC). The mean MDA, SOD, GSH-Px and CAT levels in the patient group were significantly higher than those in the control group. There was a positive correlation between LSAC scores and MDA, SOD, GSH-Px and LSAC levels, and between the duration of illness, and MDA, SOD and CAT levels in the patient group. In conclusion, our results suggest that there may be a relationship between increased antioxidant enzyme levels and MDA, and SP.

Keywords: Social phobia; Antioxidant enzyme; MDA

1. Introduction

Free radicals, with an unpaired electron in one of their orbits, are chemical species produced in many different ways, such as activation of phagocytes and the general immune system, lipid peroxidation, electron transport system in mitochondria, ischemia and trauma (Gutteridge, 1995). Free radicals have relatively short half-lives, and thus the determination of their levels is difficult. Therefore, they can be evaluated indirectly by measurement of some antioxidant enzyme levels such as superoxide dismutase (SOD), catalase (CAT) or glutathione peroxidase (GSH-Px), by products of lipid peroxidation such as malondialdehyde (MDA) or by some transition metal levels such as copper, zinc and iron (Leff, 1994). Predominantly superoxide, hydroxyl ion and nitric oxide are generated under physiological conditions during aerobic metabolism (Mahadik and Mukherjee, 1996). A small portion of the free radicals are involved in physiological processes, but the remainder are inactivated by antioxidant enzyme systems (Burton and Ingold, 1989). When free radicals are generated in excessive

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amounts or the enzymatic and nonenzymatic antioxidant defense systems are inefficient, some chain reactions causing cellular injury or even death of cells are activated (Stadtman, 1992).

Free radical damage has been investigated in the pathophysiology of neuropsychiatric disorders. There are numerous studies indicating that free radical-mediated neuronal dysfunction may be implicated in the pathophysiology of schizophrenia (Mahadik and Mukherjee, 1996). Buckman et al. (1987) reported that patients with chronic schizophrenia had levels of GSH-Px activity similar to those in healthy controls. Increased SOD activity levels in schizophrenia have been reported (Lohr, 1991). In addition, it has been suggested that patients with major depression, especially melancholia, show elevated antioxidant enzyme levels and lipid peroxidation (Bilici et al., 2001).

Another neuropsychiatric disorder in which free radicals might play a role is social phobia (SP). To the best of our knowledge, there has not yet been a study evaluating the association between free radicals and SP. Therefore, in the present study, we hypothesized that oxidative damage and antioxidant enzyme activity levels could be implicated in SP.

2. Methods

2.1. Subjects and clinical evaluation

The sample comprised 18 patients (aged 18–49 years) who had presented at the Department of Psychiatry of Firat University School of Medicine. The patients had been diagnosed with SP according to DSM-III-R criteria and met the admission criteria for the study. Written consent to participate in the study was obtained from the subjects after they were thoroughly informed about the research details. The research protocol was approved by the Firat University School of Medicine Ethics Committee.

All subjects had been free of all medications for at least the previous 2 weeks. Each patient underwent diagnostic evaluation by one trained psychiatrist using the Structured Interview for DSM-III-R Outpatient Form (SCID-OP) (Spitzer et al., 1987). Patients with Axis I comorbidity were excluded, but patients with comorbid Axis II disorders were accepted for study. In the patient population, there were six patients with personality disorder (avoidant personality disorder in three patients, obsessive-compulsive personality disorder in two patients and dependent personality disorder in one patient) and no mental retardation as an axis II disorder. All subjects were evaluated by a semistructured form that summarized information about, for example, gender, age, marital status, education, socioeconomic status, and duration of illness. Liebowitz's 24-item Social Anxiety Scale (LSAC) (Liebowitz, 1987) was used to assess the patients' level of social fear and avoidance.

Eighteen healthy control subjects were chosen among the hospital staff. Controls were interviewed with the nonpatient version of the SCID (SCID-NP) to exclude any Axis I disorder (Spitzer et al., 1990).

All subjects underwent physical and neurological examinations, as well as liver and kidney function tests. Subjects with normal results and without exclusionary criteria were admitted to the study. Exclusionary criteria were as follows: alcohol and substance abuse or dependence; presence of a severe organic condition such as Wilson's disease, Down's syndrome, malnutrition, pregnancy, diabetes mellitus, chronic renal failure, cancer, liver cirrhosis, and thyroid disease, treatment with glucocorticoids, anticonvulsants, oral contraceptives, psychotropic drugs and any antioxidant agents such as vitamins (i.e. vitamins E and C), xantine oxidase inhibitors (allopurinol, folic acid), and non-steroidal anti-inflammatory drugs; presence of epilepsy and severe neurologic disorder such as Parkinson, Huntington, and Alzheimer diseases; presence of infectious disease and excessive obesity.

2.2. Blood sampling

Venous blood samples from a left forearm vein were collected into 5-ml vacutainer tubes containing potassium EDTA between 7 and 8 a.m. after overnight fasting. Some hematological parameters were measured with an auto-analyzer (Coulter Max M, Coulter Electronics Ltd, Luton, UK). The data on smoking were obtained from each patient using a questionnaire administered 1 day before blood drawing. Eleven of the patients and nine of the controls were smokers. Nine of eleven smoker patients had >20 cigarettes per day except for two patients who had between 10 to 20 cigarettes per day. On the other hand, eight of nine smoker controls had >20 cigarettes per day while one had 10 to 20 cigarettes per day. The mean durations for smoking in smoker patients and controls were 7.47±4.62 and 6.91±4.23 years, respectively. Smoking was not permitted after 23.00 h, one day before blood drawing. The prohibition against smoking on the day before the blood drawing had been specified in the consent process.

The blood samples were centrifuged at 4000 rpm for 10 min at 4 °C to remove plasma. The buffy coat on the erythrocytes sediment was separated carefully after