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Original Article

Alterations in Redox System Parameters in Obsessive-Compulsive Disorder

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Abstract

Introduction: Obsessive-compulsive disorder (OCD) is a chronic neuropsychiatric condition characterized by intrusive obsessions and repetitive compulsions, significantly impairing daily functioning and the quality of life. Increasing evidence suggests that oxidative stress may play an important role in the pathophysiology of OCD, but the biochemical mechanisms underlying this relationship require further elaboration. This study aims to investigate the oxidant-antioxidant status in OCD patients compared to the healthy controls.

Methods: A total of 40 OCD patients diagnosed according to the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) and 40 age- and sex-matched healthy controls were included in the study. Blood samples were collected from all the participants and a spectrophotometer was used to measure levels of lipid peroxidation (LPO), superoxide dismutase (SOD) activity, and glutathione S-transferase (GST).

Results: The results of our study showed that LPO levels increased ($p \leq 0.0001$) while SOD and GST activities decreased ($p \leq 0.0001$) in OCD patients when compared to the healthy controls. These findings suggest that oxidative stress imbalance may contribute to the neurobiological mechanisms of OCD, supporting the hypothesis that increased oxidative damage and impaired antioxidant defense systems are involved in the disorder's pathophysiology of OCD.

Conclusions:. This study contributes to the growing literature on oxidative stress in psychiatric disorders and highlights the importance of investigating the biochemical pathways that may underline OCD pathogenesis. Understanding these biochemical alterations could provide valuable insights into the molecular basis of OCD and may led to the new approaches for potential therapeutic targets.

Keywords: Obsessive-compulsive disorder, oxidative stress, antioxidant enzymes, lipid peroxidation

1. Introduction

Obsessive-compulsive disorder (OCD) is a chronic and debilitating mental health condition characterized by the presence of obsessions and/or compulsions, as defined by the American Psychiatric Association in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) (1). Obsessions are recurrent, persistent, and intrusive thoughts, urges, or images that cause considerable anxiety or distress. Compulsions, on the other hand, are repetitive behaviors or mental actions performed in response to an obsession or according to strict rules, aimed at reducing distress or preventing a feared event or situation (2). Common obsession types include contamination fears, harm-related thoughts, and symmetry or ordering concerns, while compulsions often involve excessive cleaning, checking, or counting behaviors (3). The prevalence of OCD is estimated to be approximately 1-3% globally, with significant variations across populations, and it frequently leads to substantial impairments in social, occupational, and overall quality of the life (3, 4).

The etiology of OCD is multifactorial, involving a complex interaction of environmental, familial, and genetic-epigenetic factors (5). Environmental triggers such as infections, trauma, or stress have been associated with the onset or exacerbation of symptoms in predisposed individuals. Familial studies indicate a higher prevalence of OCD among first-degree relatives of affected individuals, suggesting a strong hereditary component (6). Furthermore, genetic and epigenetic mechanisms, including variations in genes related to serotonergic, dopaminergic, and glutamatergic systems, have been implicated in the pathophysiology of the disorder (7). Emerging evidence highlights the role of oxidative stress and neuroinflammation in neuropsychiatric disorders. These findings provide new pathways for understanding the biological basis of OCD (8, 9).

On the otherhand, oxidative stress arises from an imbalance between the production of reactive oxygen species (ROS) and the antioxidant defense systems (10). This imbalance can lead to lipid peroxidation, protein oxidation, and DNA damage, which have been linked to neuropsychiatric disorders, including OCD (11). Malondialdehyde (MDA), a marker of lipid peroxidation, serves as an indicator of oxidative stress levels. Enzymatic antioxidants, such as glutathione S-transferase (GST), and superoxide dismutase (SOD), play pivotal roles in mitigating oxidative damage by neutralizing ROS (12). Dysregulation of these systems has been reported in various psychiatric conditions and it is hypothesized to contribute to the pathophysiology of OCD through mechanisms such as neuronal damage, synaptic dysfunction, and altered neurotransmitter metabolism (9).

The investigation of oxidant-antioxidant enzyme systems and lipid peroxidation levels in OCD patients is crucial for elucidating the potential role of oxidative stress in the OCD. By comparing these parameters between OCD patients and healthy controls, the present study aims to provide insights into the biochemical alterations associated with OCD. Understanding these mechanisms may not only enhance our knowledge of the etiology of the disease, but may also pave the way for the development of novel therapeutic strategies targeting oxidative stress pathways. This study may contribute to the literature investigating the relationship between oxidative stress and psychiatric disorders and may offer potential biomarkers for monitoring the diagnosis and treatment of OCD in the future.

2. Methods

2.1. Selection of study groups

The patient group consisted of 40 OCD patients which admitted to Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine, Department of Psychiatry, Istanbul, Türkiye, and diagnosed with OCD according to DSM-V diagnostic criteria (1). The ethnic identity of the OCD patients included in the study was Turkish. OCD patients with comorbid psychiatric disorders were not included in the study. The patient group consisted of 22 female and 18 male volunteers, and the mean age was 30.32 ± 10.38 years. The severity of the disease was determined by the Yale-Brown Obsessive

Compulsive Scale (Y-BOCS) administered to OCD patients (3). The control group was selected among healthy individuals who applied to Istanbul University-Cerrahpasa ,Cerrahpasa Faculty of Medicine Hospital for regular health screening. The control group consisted of 40 healthy Turkish volunteers among of whom 25 were females and 15 males, with a mean age of 32.00 ± 10.92 years. Volunteers with a previous diagnosis of psychiatric disorder were excluded from the control group. The study groups consisted of volunteers aged 18-55 years. The procedures to be performed on the blood samples were explained to each individual in the patient and control groups and informed consent forms were obtained to voluntarily agree to participate in this study.

2.1.1. Yale-Brown obsessive compulsive scale (Y-BOCS)

Y-BOCS is a 10-question scale designed to measure the severity and type of symptoms in people with OCD. This scale was validated by Goodman et al. who reported that the Y-BOCS was significantly correlated with OCD. According to the result of this scale, the patient has a disease severity score between 0–40. Total scores can be split five categories, based on the severity of the symptoms. A score of less than 7 subclinical, 8–15 mild, 16–23 moderate, 24–31 severe, and 32–40 extreme OCD severity (3).

2.1.2. Sociodemographic questionnaire

A sociodemographic questionnaire was applied to the study groups, questions such as age, ethnicity, age of onset of OCD, medication use and family history were asked.

2.2. Biochemical analysis

Venous blood samples were collected in EDTA tubes from each volunteer in the study groups. The blood in the anticoagulated tubes was centrifuged at 2500 rpm, 4 °C for 20 minutes. The plasma remaining at the top of the tube at the end of centrifugation was collected in 1.5 ml Eppendorf tubes. It was stored at -80 °C until biochemical methods were performed.

2.2.1. Assay of the Total Protein Content

The plasma protein levels were measured in order to evaluate the biochemical analyses per mg of protein by Lowry method (13).

2.2.2. Determination of LPO

LPO measurement was made based on the absorbance obtained by reading the color change resulting from the reaction of Malondialdehyde (MDA), the product of this reaction, with thiobarbituric acid at 532 nm spectrophotometrically (14).

2.2.3. Measurement of SOD and GST Enzyme Activities

SOD activity was measured depending on the increase in the photooxidation rate of riboflavin-sensitized o-dianisidine. Under the influence of fluorescence light, the superoxide radical formed by riboflavin was converted to H_2O_2 by the catalysis of SOD in the environment. The formed H_2O_2 reacts with o-dianisidine to form a colored product, and the absorbance was measured at 460 nm spectrophotometrically depending on this color (15).

Glutathione *S*-transferase (GST) activity was evaluated by measuring the absorbance of the product formed by the conjugation of Glutathione (GSH) with 1-chloro-2,4-dinitro-benzene at 349 nm spectrophotometrically (16).

2.3. Statistical Analysis

Data was presented as mean ± standard deviation. The differences between the parameters investigated were tested by using unpaired samples Student t-test. Differences with p-values of 0.05 or less were considered significant. Statistical analysis was performed with Graph-Pad version 10.

3. Results

LPO was evaluated by measuring malondialdehyde (MDA) levels in plasma. The result of LPO comparison between the groups was-given in Fig 1. MDA levels were significantly higher in the OCD group when compared with the control group ($p \leq 0.0001$).

The results of SOD activity were given in Fig 2. SOD activity decreased significantly in the OCD group when compared to the control group (p≤0.0001).

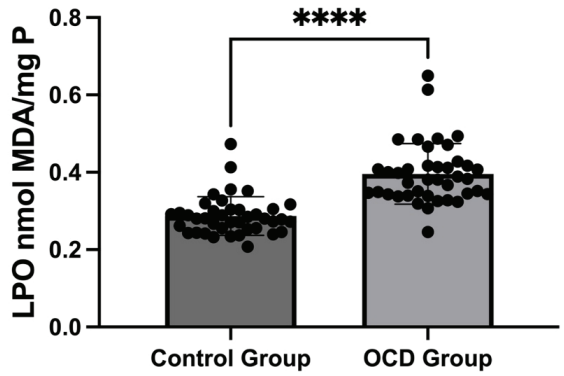

Figure 1. Comparison of lipid peroxidation (LPO) in terms of malondialdehyde (MDA) levels in plasma samples. n=40; ****p≤0.0001 significantly different.

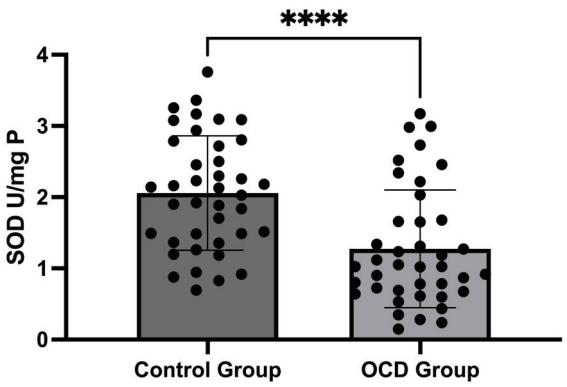

Figure 2. Comparison of superoxide dismutase activities in plasma samples. n=40; ****p≤0.0001 significantly different.

A comparison of GST activity between the two groups was in Fig 3. Consistent with increased LPO and decreased SOD activities, decreased GST activity was found in the OCD group when compared with the control group (p≤0.0001).

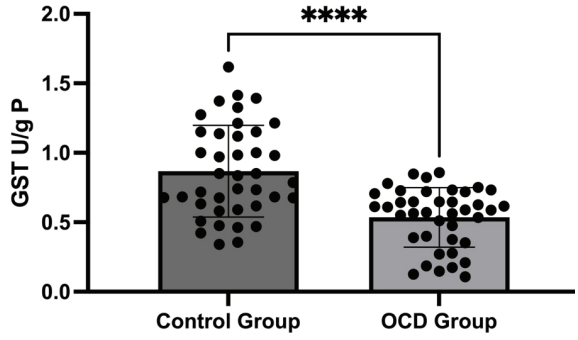

Figure 3. Comparison of glutathione S-transferase activities in plasma samples. n=40; ****p≤0.0001 significantly different.

4. Discussion

The results of the present study showed that the oxidant-antioxidant status in OCD patients was disrupted. In the literature, conflicting results have been reported regarding MDA levels in studies on OCD, and these studies also have various limitations (17). Jiménez-Fernández et al. and Liu et al. showed that MDA levels were higher in groups with depression when compared to the healthy controls (18, 19). Other studies have also reported that MDA levels were higher in groups with psychological disorders when compared to the healthy controls (20, 21). However, unlike these studies, Ranjekar et al. showed that MDA levels in the serum of schizophrenia patients did not reveal any difference when compared to the healthy controls (22). Furthermore, Talarowska et al. also stated that plasma MDA levels of depressive disorders was not statistically significant from the healthy controls (23). In the present study, it was found that LPO was increased through MDA levels in the plasma of OCD patients. In conclusion, it was found that LPO increased in the plasma of OCD patients when compared to the healthy control groups.

As it is known, ATP production by electron transport chain in mitochondria or respiratory burst of macromolecules in macrophages and neutrophils causes oxidative stress. Overcoming antioxidant capacity by ROS causes damage to macromolecules, neurotransmitters, and DNA. Furtherly, neurotransmitters such as dopamine, serotonin, gamma-aminobutyric acid (GABA), and glutamate have a regulatory role in OCD (21). A change in the synthesis or mechanism of these neurotransmitters could increase oxidative stress in the central nervous system (24). Brambilla et al. reported that in their study that MDA levels reduce serotonin levels (25). These results may allow the establishment of a relationship between MDA and OCD by associating MDA levels with neurotransmitters that are important in OCD.

The production of ROS can physiologically cause neurophysiological responses by causing neurotransmitter disruption and increased blood–brain barrier permeability. This results in neuroinflammation and cell death (26, 27). OCD is commonly seen in individuals with mitochondrial

dysfunction due to genetic disorders, and it has been reported that oxidative stress is high in these patients. In addition, increased ROS may cause peroxidation in membrane lipids and disrupt membrane integrity.

Under normal conditions, there is a balance between the oxidant-antioxidant system. In order to ensure this balance, various antioxidant enzymes such as SOD and CAT are present in the organism. With the increase in the oxidant species, the defense system in the organism is triggered and antioxidant enzymes are activated. Özdemir et al. repoted that SOD activity increased in OCD patients compared to controls (17). It is thought that there is an increase in the levels of oxidative species in OCD, and the antioxidant system is triggered in response to this situation and there may be an increase in the activities of antioxidant enzymes such as SOD. In the present study, the decrease in SOD activity in the plasma of OCD patients compared to the healthy control group may be an indication that the defense mechanism in the body is active but insufficient when compared to ROS.

Also it is kown that, GST is an important enzyme that catalyzes the conjugation of reduced GSH to xenobiotic substrates for detoxification purposes (28, 29). The activation of the antioxidant system in response to increased oxidative stress may also cause changes in GST activity. Quadros et al. revealed increased GST activity in anxiety-like behaviors induced zebrafish brains compared to the control group (30). In contrast to this study, the current study found that GST activity was decreased in OCD groups compared to the control group. As far as we know, GST activity has not been measured in OCD patients before. Therefore, the decrease in the GST activity measured in the plasma of OCD patients in our study may be important data for future studies.

5. Conclusion

In our study, redox system parameters were evaluated by measuring MDA levels, GST, and SOD activities in the plasma of OCD patients. As a result of our study, it could be stated that the oxidant-antioxidant balance in the plasma of OCD patients is disrupted. In future studies, the pathways of various neurotransmitters (serotonin, glutamate, GABA and dopamine), which are thought to have an important role in OCD, can be investigated and the relationships between these neurotransmitters and oxidant-antioxidant balance can be evaluated.

Conflicts of interest: The authors declare no conflicts of interest related to this work

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Ethics approval: This study was approved by the ethics committee of the Cerrahpaşa Faculty of Medicine, Istanbul, Türkiye (issue no: E-83045809-604.01.02-70153) and conducted in accordance with the principles of the Declaration of Helsinki.

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