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Review article

Oxidative Stress and Antioxidant Defense in Obsessive-Compulsive Disorder: Focus on Catalase Gene Variability

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Abstract: Obsessive-compulsive disorder (OCD) is a chronic and disabling psychiatric disorder characterized by intrusive obsessions and repetitive compulsions. Although serotonergic and cortico-striato-thalamo-cortical circuit dysfunctions are well established in OCD pathophysiology, emerging evidence highlights the role of oxidative stress in its neurobiological mechanisms. Oxidative imbalance results from excessive production of reactive oxygen species (ROS) relative to antioxidant defense capacity, leading to neuronal dysfunction, lipid peroxidation, mitochondrial impairment, and altered neurotransmission. Catalase (CAT), a key antioxidant enzyme, detoxifies hydrogen peroxide and maintains redox homeostasis in the central nervous system. Genetic polymorphisms in the CAT gene may influence enzyme activity and modulate susceptibility to oxidative damage. This review summarizes current evidence regarding oxidative stress in OCD, the biological significance of catalase in the brain, and the potential contribution of CAT genetic variability to OCD pathogenesis.

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Introduction

Obsessive-compulsive disorder (OCD) is a chronic psychiatric condition characterized by recurrent intrusive thoughts (obsessions) and repetitive behaviors or mental rituals (compulsions) performed to alleviate distress [1]. These symptoms are time-consuming and cause significant impairment in social, occupational, and daily functioning [2].

The etiology of OCD is complex and multifactorial, involving genetic vulnerability, environmental stressors, and neurobiological dysregulation [3]. While serotonergic dysfunction and abnormalities within cortico-striato-thalamo-cortical (CSTC) circuits remain central explanatory models, growing evidence suggests that oxidative stress may represent an additional mechanistic pathway contributing to disease development [4].

Oxidative stress arises when reactive oxygen species (ROS) production exceeds the capacity of antioxidant defense systems, leading to cellular and molecular damage [5]. Given the brain's high oxygen consumption and lipid-rich composition, it is particularly vulnerable to oxidative injury. Among antioxidant enzymes, catalase (CAT) plays a critical role in detoxifying hydrogen peroxide (H_2O_2), thereby protecting neurons from oxidative damage [6]. Genetic variations in the CAT gene may influence enzyme expression and activity, potentially contributing to psychiatric vulnerability.

Clinical and Epidemiological Overview of OCD

OCD affects approximately 2–3% of the global population and typically manifests during late adolescence or early adulthood, although childhood onset is common [7]. The disorder affects both sexes, though onset tends to occur earlier in males.

According to the Diagnostic and Statistical Manual of Mental Disorders (5th ed.; DSM-5), OCD is diagnosed when obsessions and/or compulsions are time-

consuming (more than one hour per day) or cause clinically significant distress or impairment [2].

OCD is clinically heterogeneous and can be categorized into several symptom dimensions [7, 8]. These dimensions are summarized in **Table 1**.

The heterogeneity of OCD symptom dimensions suggests partially distinct neurobiological mechanisms. Increasing evidence indicates that biological factors, including oxidative stress markers, may vary across symptom subtypes, highlighting the need to explore molecular contributors such as antioxidant enzyme variability [9].

Table 1. Major Symptom Dimensions in Obsessive-Compulsive Disorder.

Symptom Dimension	Core Obsessions	Typical Compulsions
Contamination	Excessive fears of dirt, germs, toxins, or illness	Repeated washing, cleaning, showering, avoidance behaviors
Harm/Checking	Fear of causing harm to oneself or others; fear of mistakes	Repeated checking (locks, appliances), reassurance seeking
Unacceptable/Taboo Thoughts	Intrusive aggressive, sexual, or religious thoughts	Mental rituals, praying, neutralizing thoughts
Symmetry/Ordering	Preoccupation with symmetry, exactness, or "just-right" feelings	Ordering, arranging, counting, repeating
Hoarding	Persistent difficulty discarding possessions	Accumulation of items, distress when discarding

Genetic Basis of OCD

Family and twin studies demonstrate a significant hereditary component in OCD. First-degree relatives of affected individuals have an elevated risk compared to the general population [10]. Heritability estimates are particularly high in early-onset OCD.

Genetic studies have implicated multiple pathways, including serotonergic, dopaminergic, glutamatergic, inflammatory, and oxidative stress-related genes. However, OCD is considered polygenic, with individual variants exerting modest effects [3].

Oxidative Stress: Biological Mechanisms

Oxidative stress occurs when ROS production surpasses antioxidant capacity [11]. Major ROS include superoxide anion, hydrogen peroxide, and hydroxyl radicals. These molecules are generated primarily through mitochondrial respiration but also through NADPH oxidase activity and peroxisomal metabolism [12].

Under physiological conditions, ROS participate in cell signaling and immune regulation [9]. However, excessive ROS leads to:

- Lipid peroxidation (e.g., malondialdehyde formation)
- Protein oxidation
- DNA damage (e.g., increased 8-OHdG)
- Mitochondrial dysfunction
- Neuroinflammatory activation

The brain's high lipid content and metabolic rate make it especially susceptible to oxidative injury [13].

Oxidative Stress in Psychiatric Disorders

Elevated oxidative stress markers have been consistently reported in major depressive disorder, schizophrenia, and bipolar disorder [14]. Increased lipid peroxidation products and decreased antioxidant enzyme activities—including superoxide dismutase (SOD), catalase, and glutathione peroxidase (GPx)—have been observed [15].

Emerging evidence suggests similar redox dysregulation in OCD. Studies report increased oxidative markers and reduced total antioxidant capacity in affected individuals [4]. These findings suggest that oxidative imbalance may contribute to neuronal dysfunction within CSTC circuits implicated in OCD [9].

Catalase: Structure and Function

Catalase is a heme-containing antioxidant enzyme primarily localized in peroxisomes. It catalyzes the decomposition of hydrogen peroxide into water and oxygen through a highly efficient two-step reaction [16].

By detoxifying hydrogen peroxide, catalase:

- Prevents formation of highly reactive hydroxyl radicals

- Reduces lipid peroxidation
- Protects DNA and proteins
- Preserves mitochondrial integrity

Although primarily peroxisomal, catalase influences overall cellular redox balance and indirectly modulates neurotransmitter metabolism [9].

Catalase in the Central Nervous System

In the central nervous system, catalase contributes to neuronal protection against oxidative damage. Reduced catalase activity has been observed in neurodegenerative disorders and mood disorders [17].

Hydrogen peroxide accumulation can influence monoaminergic systems by altering serotonin and dopamine metabolism. Therefore, impaired catalase activity may indirectly affect neurotransmission relevant to OCD pathophysiology [9].

Catalase Gene Polymorphisms and Psychiatric Vulnerability

Genetic polymorphisms, particularly single nucleotide polymorphisms (SNPs), contribute to interindividual variability in enzyme activity [18]. Variants in promoter regions may alter transcription factor binding and gene expression levels.

Functional polymorphisms in the CAT gene have been associated with altered enzyme activity in various diseases [9]. Reduced catalase expression may result in increased hydrogen peroxide accumulation, promoting oxidative DNA damage, neuroinflammation, and synaptic dysfunction.

Although research directly examining CAT polymorphisms in OCD is limited, findings from related psychiatric disorders suggest that antioxidant gene variability may influence susceptibility to redox-mediated neuronal dysfunction [9].

Gene–Environment Interaction

Environmental stressors such as psychological stress, infections, and toxin exposure increase ROS production [19]. Individuals carrying less efficient antioxidant variants may exhibit heightened vulnerability under oxidative challenge.

This gene–environment interaction model may help explain the heterogeneity in OCD severity, symptom dimensions, and treatment response [9].

Therapeutic Implications and Future Directions

Understanding oxidative mechanisms in OCD opens potential therapeutic avenues. Antioxidant-based interventions, including N-acetylcysteine and catalase mimetics, have shown preliminary promise in modulating redox balance [9].

Future research should focus on:

- Large-scale genetic association studies of antioxidant genes
- Integration of oxidative biomarkers with neuroimaging
- Symptom-dimension-specific molecular profiling
- Precision psychiatry approaches targeting redox pathways

Conclusion

OCD is a multifactorial disorder in which oxidative stress may contribute to neurobiological dysfunction. Catalase plays a central role in maintaining neuronal redox balance by detoxifying hydrogen peroxide. Genetic variability in the CAT gene may influence antioxidant capacity and vulnerability to oxidative damage. While direct evidence in OCD remains limited, converging data from psychiatric research support further investigation into catalase as a potential molecular contributor to OCD pathogenesis.

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