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Mini Review

Growth Factors, Cell Receptors, Intracellular Kinases, and Transcription Factors Associated with Obsessive Compulsive Disorder (OCD)

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Abstract

Obsessive-Compulsive Disorder (OCD) is a complex psychiatric condition characterized by obsessions and compulsions. Research has delved into the neurobiological underpinnings of OCD. This review focuses on growth factors, cell receptors, intracellular kinases, and transcription factors that may be associated with the etiology of OCD.

Keywords: Obsessive-Compulsive Disorder (OCD); Gamma Aminobutyric Acid (GABA)

Growth factors associated with OCD

Obsessive-Compulsive Disorder (OCD) is a complex neuropsychiatric condition characterized by intrusive thoughts (obsessions) and repetitive behaviors (compulsions). Research has increasingly focused on understanding the underlying biological factors associated with OCD, including the role of growth factors such as Brain-Derived Neurotrophic Factor (BDNF) [1]. BDNF is a neurotrophin that plays a crucial role in neuronal survival, growth, and differentiation, and its dysregulation has been implicated in various psychiatric disorders, including OCD [2]. Studies have identified significant associations between BDNF gene polymorphisms, such as rs2883187 and the Val66Met variation, and OCD [3,4]. These genetic variations in BDNF may influence the risk of developing OCD and contribute to the heterogeneity of the disorder [3,4].

In addition to BDNF, Hepatocyte Growth Factor (HGF) and Gamma Aminobutyric Acid (GABA) have been found to be significantly decreased in individuals with Obsessive-Compulsive Disorder (OCD) [5].

Furthermore, the interaction between BDNF and other neurotransmitter systems, such as serotonin, has been highlighted in the context of OCD [6] (Paribello, 2023). Serotonin is a key neurotransmitter involved in mood regulation and has been a primary target for pharmacological interventions in OCD. The comorbidity of anxiety and affective disorders with OCD underscores the complex interplay of neurotransmitter systems in the pathophysiology of the disorder [6]. Additionally, studies have shown that BDNF levels may differ between individuals with OCD and healthy controls, suggesting a potential role for BDNF in the pathogenesis of OCD [7].

Animal models have also provided insights into the neurobiological mechanisms underlying OCD. Dysfunction in cortico-striato-thalamo-cortical (CSTC) circuits, dysregulated synaptic transmission, and altered signaling pathways, such as

the TrkB/ERK-MAPK pathway, have been implicated in OCD-like behaviors [8]. These findings suggest that aberrant neural circuitry and molecular signaling pathways contribute to the manifestation of OCD symptoms.

Moreover, the gut-brain axis has emerged as a novel area of research in understanding psychiatric disorders, including OCD. The gut microbiota has been implicated in the pathophysiology of OCD, with potential implications for novel therapeutic approaches [9]. Changes in the gut microbiome can influence neuroimmune responses and neurotransmitter signaling, which may impact the development and progression of OCD symptoms.

Epigenetic studies have also shed light on the role of DNA methylation in OCD. Alterations in DNA methylation patterns, particularly in genes related to neurotransmitter systems and neurodevelopmental pathways, have been associated with OCD [10]. These epigenetic changes may provide valuable insights into the biological underpinnings of OCD and could serve as potential biomarkers for the disorder.

In addition to genetic and epigenetic factors, neurotrophic factors like Insulin-Like Growth Factor-1 (IGF-1) have been implicated in OCD. Studies have shown alterations in peripheral BDNF levels in individuals with OCD, suggesting a dysregulation of neurotrophic factors in the disorder. The dysregulation of growth factors like BDNF and IGF-1 may contribute to the pathophysiology of OCD and could be targeted in the development of novel treatment strategies.

Overall, the multifactorial nature of OCD involves a complex interplay of genetic, neurobiological, and environmental factors. Understanding the role of growth factors, neurotransmitter systems, neural circuits, and the gut-brain axis in OCD pathogenesis is crucial for developing targeted interventions and personalized treatment approaches for individuals with OCD.

Cell receptors associated with OCD

Research on OCD has delved into neurobiological underpinnings, focusing on various neurotransmitter systems that play a role in its pathophysiology. Serotonin, dopamine, and glutamate have been implicated in the development and progression of OCD [11-13]. The orbitofronto-striatal model has been revisited to understand the neural pathways involved in OCD, highlighting the importance of the frontal lobe and neostriatum [14]. Additionally, the endocannabinoid system has emerged as a potential player in the pathophysiology of OCD, alongside classical neurotransmitter systems [15].

Studies have shown that serotonin, a key neurotransmitter, is central to the pharmacological treatment of OCD [16]. However, the involvement of other neurotransmitters beyond serotonin, such as dopamine, is also crucial in the pathogenesis of OCD [12,17]. The dopaminergic system interacts with serotonin pathways to enhance the efficacy of treatments in OCD [17]. Furthermore, glutamate, the primary excitatory neurotransmitter in the cortico-striatal-thalamo-cortical circuits implicated in OCD, has been a focus of research for potential therapeutic strategies [13].

The role of neurotransmitters extends to animal models of OCD, where serotonin, dopamine, and glutamate receptors have been identified as key players in the disorder's pathology [12,18]. The intricate interplay between these neurotransmitter systems is evident in the complex neural circuits involved in OCD, such as the cortico-striato-thalamo-cortical loop [12,18]. Moreover, the involvement of GABA, the primary inhibitory neurotransmitter, has been suggested in OCD, influencing sleep, relaxation, and excitation levels [19,20].

Deep brain stimulation (DBS) has emerged as a potential therapeutic approach for OCD, with its effects possibly mediated through the manipulation of serotonergic pathways [21]. The nucleus accumbens (NAc), a target for DBS in OCD, receives input projections from various neurotransmitter systems, including dopaminergic, serotonergic, histaminergic, cholinergic, and glutamatergic projections [22].

Genetic studies have also shed light on the involvement of specific genes and receptors in OCD. Variants of genes related to glutamatergic pathways, such as the glutamate receptor GRIK2, have been associated with OCD susceptibility [23,24]. Furthermore, the serotonin transporter and receptor subtypes implicated in OCD are highly expressed in the ventral striatum, influencing the functioning of cortico-striatal circuits [25].

In conclusion, OCD is a multifaceted disorder influenced by a network of neurotransmitter systems. While serotonin has been a primary focus in OCD research, the involvement of dopamine, glutamate, GABA, and other neurotransmitters is crucial in understanding the complex pathophysiology of the disorder. The interplay between these neurotransmitter systems within neural circuits underscores the need for comprehensive approaches to target multiple pathways for effective OCD treatment.

Intracellular kinases associated with OCD

The pathophysiology of OCD involves intricate interactions between various neurotransmitter systems and intracellular signaling pathways. One crucial aspect of OCD research focuses on the involvement of intracellular kinases in the development and maintenance of the disorder [26]. Intracellular kinases are key signaling molecules that regulate cellular processes by phosphorylating target proteins, thereby modulating their function. In the context of OCD, several intracellular kinases have been implicated, including protein kinase G (PKG), protein kinase C (PKC), and p38 mitogen-activated protein kinase (p38 MAPK) [26].

Studies have shown that dysregulation of intracellular signaling pathways, such as those involving protein kinases, can contribute to the pathogenesis of OCD. For instance, alterations in calcium-calmodulin-dependent protein kinase II activity have been linked to autoimmune-mediated changes in neuronal signaling, potentially underpinning the behavioral and motor symptoms observed in neuropsychiatric disorders like OCD and tic disorders [27]. Furthermore, the serotonin transporter (SERT), a protein crucial in serotonin reuptake, is regulated by various intracellular signaling cascades, highlighting the intricate interplay between neurotransmitter systems and intracellular kinases in OCD pathology [28].

Intracellular kinases play a vital role in mediating the effects of neurotransmitters like serotonin, which have been implicated in the pathophysiology of OCD. Serotonin, known for its role in mood regulation and anxiety, interacts with intracellular signaling pathways to modulate neuronal activity and synaptic transmission. Dysregulation of these pathways, including the activity of protein kinase C (PKC) and protein kinase A (PKA), has been associated with OCD [29]. Moreover, the involvement of cyclic adenosine monophosphate (cAMP) signaling, regulated by protein kinase A (PKA), has been suggested in OCD, indicating the significance of intracellular signaling mechanisms in the disorder [29].

The role of intracellular kinases in OCD extends beyond neurotransmitter regulation to encompass broader cellular functions. For example, studies have highlighted the impact of intracellular signaling pathways on neural circuitry implicated in OCD, such as the orbitofronto-striato-thalamic circuit and regions like the insula and cerebellum [30]. These findings underscore the intricate interplay between intracellular kinases, neural circuits, and neurotransmitter systems in the pathophysiology of OCD.

Furthermore, research has indicated a potential link between immune system activation and neuropsychiatric disorders like OCD. The immune system, through the release of cytokines and inflammatory mediators, can influence neurotransmission and neuronal signaling pathways associated with OCD [26]. This interaction between the immune system and intracellular signaling cascades may provide novel insights into the etiology of OCD and the potential role of immune-related intracellular kinases in the disorder.

In conclusion, the involvement of intracellular kinases in OCD represents a critical area of research that sheds light on the complex interplay between cellular signaling pathways, neurotransmitter systems, and neural circuitry in the pathophysiology of the disorder. Understanding how intracellular kinases modulate neuronal function and contribute to OCD symptoms may pave the way for the development of targeted therapeutic interventions that aim to restore the balance of intracellular signaling pathways in individuals with OCD.

Transcription factors associated with OCD

The etiology of OCD is multifaceted, involving genetic inheritance, psychological factors, and environmental influences [31]. Research has shown a significant association between autoimmunity and primary OCD, indicating a potential role of immune system dysregulation in the development of the disorder [32]. Moreover, studies have highlighted the impact of genetic predisposition, environmental factors such as education and marital status, employment, and intrinsic factors like age on the

prevalence and severity of OCD [33]. Additionally, the presence of OCD cases following head trauma, response to serotonin reuptake inhibitors, and surgical interventions underscore the importance of biological factors in the development and treatment of OCD [34].

Cognitive factors play a crucial role in OCD, with dysfunctional beliefs acting as risk and maintaining factors for the disorder [35]. Studies have established the central role of cognitive factors such as thought action-fusion and perfectionism in the manifestation of obsessive-compulsive symptoms [36]. Furthermore, the presence of early maladaptive schemas in OCD patients suggests a familial and genetic basis for these schemas, emphasizing the need for further investigation with larger sample sizes [37]. Insight into the disorder is also essential, as patients with poor insight tend to exhibit more severe symptoms and have a higher likelihood of comorbid psychiatric conditions [38].

Neurobiological factors are integral to understanding OCD, with studies indicating patient-specific intracranial neural signatures associated with obsessions and compulsions in the ventral striatum [39]. This suggests that closed-loop stimulation targeting specific neural circuits may offer a promising treatment approach for OCD. Moreover, neuroimaging studies have confirmed the biological basis of OCD, highlighting abnormalities in brain structure and function [40]. The deficiency in cognitive functions, particularly response inhibition, has been identified as a major pathological factor in OCD, contributing to the core symptoms of the disorder [41].

The COVID-19 pandemic has had a significant impact on the prevalence of OCD, with studies reporting an increase in OCD incidents during the epidemic [42]. Specific obsessions related to contamination and compulsions such as cleaning and washing have been noted to be significantly higher during this period. Additionally, changes in the gut microbiota composition have been suggested to influence the severity of OCD symptoms, pointing towards a potential link between gut health and mental health disorders [43].

The relationship between OCD and other psychiatric conditions has been explored extensively. Meta-worry has been associated with various anxiety disorders, including OCD, highlighting the interconnected nature of different psychological conditions [44]. Furthermore, the overlap between pathological gambling, OCD, and obsessive-compulsive traits underscores the need to consider comorbidities when assessing and treating OCD patients [45]. The differentiation between delusions and obsessions in patients with OCD and schizophrenia poses a diagnostic challenge, emphasizing the importance of accurate assessment and differential diagnosis [46].

OCD is a complex disorder influenced by a combination of genetic, environmental, cognitive, and neurobiological factors. Understanding the intricate interplay of these factors is crucial for developing effective treatment strategies and improving outcomes for individuals with OCD. Further research into the underlying mechanisms of OCD, including immune system dysregulation, neural signatures, and cognitive processes, is essential for advancing our knowledge and enhancing therapeutic interventions for this debilitating condition.

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