

The Aetiology of Oppositional Defiant Disorder: The Gene and Environment Interaction

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Abstract. Oppositional Defiant Disorder (ODD), commonly appears during childhood and shows specific behavioral features. It is marked by frequent irritability, obvious defiant attitudes and a tendency toward vindictive actions in children. The development of ODD is closely related to the interaction between genetic and environmental factors. Recent studies have found that gene polymorphisms are linked to unusual functions of neurotransmitters in the brain. These genes include the MAOA gene, the DRD4 gene and the 5-HTT gene which regulate emotional and behavioral responses. Environmental factors also play an important role in increasing the overall risk of developing ODD in young people. These factors include experiences of childhood maltreatment and growing up in a low socioeconomic status environment. Future studies should focus on epigenetic changes and complex interactions among multiple genes and environments. This article reviews three key parts related to the etiology of Oppositional Defiant Disorder. It covers major genetic factors, common environmental risk factors and the gene-environment interaction mechanism. The paper analyzes how each factor works and interacts to contribute to the development of ODD in children. It also provides a comprehensive framework for understanding the complex nature of this behavioral disorder.

Keywords: Oppositional Defiant Disorder, Gene, Environment Factors, MAOA Gene

1. Introduction

Oppositional defiant disorder, or ODD, is defined by the DSM-V as a persistent pattern of angry and defiant behaviors which appear during interactions with at least one person. This disorder requires at least four symptoms from the categories listed in the DSM-V booklet and a duration of no less than six months. Patients with ODD are usually sensitive and easily irritated, and they also tend to annoy others and disobey those in authority positions. For children under five years old, these symptoms must appear on most days during the six-month period to be diagnosed. Children over five years old must show these symptoms at least once a week for the same six-month duration to meet the diagnostic criteria. ODD has a profound impact on the social functioning of patients which causes significant distress in their daily social interactions. The frequency of symptom occurrence and the number of locations where symptoms appear can determine the severity of ODD which is used as key diagnostic features. ODD is an antisocial behavior, or ASB, which is defined as acts that disrupt

the social and physical norms of the society. This kind of conduct is also linked to low level criminal activities and non-criminal hostile behaviors [1].

ODD is thought to occur as a result of a combination of environmental and biological influences via gene-environment interaction or G x E interaction. This interaction is concerned with two key factors namely genetic factors and environmental factors respectively. The strengths and effects of biological variables in causing ODD are different than those of environmental factors [2]. A number of genetic factors have been associated with ODD and these include the monoamine oxidase A gene, the dopamine D4 receptor gene and the 5-HTT gene. Studies show that the MAOA gene is linked to an upsurge in aggression and antisocial behaviors particularly in males bearing the low-activity allele [3]. Similarly, the variable number tandem repeat polymorphism is associated with an increased impulsivity, sensation-seeking, and aggression. This association is especially evident in the adolescence age [4]. Moreover, the 5-HTTLPR polymorphic genotype has been demonstrated to significantly contribute to development of antisocial behaviors [5]. Such genetic inclinations are usually evident in the common symptoms of ODD that comprise defiance and aggression towards others.

Nevertheless, it should be noted that genetic factors represent just one of the multifaceted causes of ODD. Environmental factors such as family and social factors are very crucial in the expression of ODD symptoms. It is important to note that childhood maltreatment is regarded as one of the leading causative factors and research has indicated that there exists a positive relationship between maltreatment experiences and ASBs in different age groups [3]. Corporal punishment is considered to be a type of maltreatment and in some studies, it has been said to cause the development of violent behaviors [6]. Moreover, socioeconomic status, or SES is also a significant factor in aetiology of ODD. Low SES families can be very hard pressed to discipline their children because of financial demands, or because of stress of the environment in high-risk communities. Moreover, the level of parental education, which is usually lower in low-SES families, may influence their capability to deliver effective discipline and guidance. This failure to offer the appropriate guidance heightens chances of children developing antisocial behaviors [7]. Consequently, people who grow up in such an environment tend to acquire behaviors that are related to ODD. The aim of this essay is to examine the genetic and environmental factors that can contribute to the development of ODD. The primary aim of it is to test the interaction between the various variables with the G x E interaction.

2. Genetic factors

2.1. The MAOA gene

The monoamine oxidase A gene, often referred to as the MAOA gene, is commonly associated with antisocial behaviors such as aggression, impulsivity, and violence. These antisocial behaviors are closely linked to Oppositional Defiant Disorder, or ODD, which is a type of antisocial personality disorder, or APD. Individuals diagnosed with ODD exhibit these antisocial behaviors as key symptoms of their condition. The MAO enzyme helps to catalyse the metabolism of biological amines, including neurotransmitters such as serotonin, norepinephrine, and dopamine [4]. These neurotransmitters are closely associated with emotion regulations, which further suggests that the MAOA gene would result in emotion-control issues which are traits of this disorder. Besides, one specific polymorphism in the promoter region of the MAOA gene is the MAOA upstream variable number tandem repeat (MAOA-uVNTR). This means there are variations among the activity level of the MAO enzyme and therefore different levels may have different effects on the behaviours

displayed. Kant et al. studied 336 clinically aggressive children and healthy controls [8]. They found that MAOA-L (long allele) variant is significantly associated with oppositional behaviours for males older than 13, and for those who are younger, the MAOA-S (short allele) variant makes a larger impact. This means this type of polymorphism is linked to the onset of ODD. Additionally, scientists have found that the 2-repeat allele of the same gene is also related to the expression of ASBs. This is further supported by Prasad et al. who found MAOA-S combining with adverse childhood experience has an increased risk of developing aggressive behaviours [9]. This means that the MAOA-S is more impactful in causing ODD, therefore, the MAOA-uVNTR has an important role in the onset of ODD.

On the one hand, the studies that investigate the effect of the MAOA gene are reliable as their samples include a wide range of participants within the age that ODD may occur, from children to young adults. Yet even the MAOA gene is seen as a significant factor in causing ODD, it may only be a predisposing factor. Primarily, all the research papers that investigate the effect of the MAOA gene discuss both the gene and environmental factors together. This means that ASBs cannot be only caused by genetic factors without the aid of environmental variables. As a result, the MAOA gene is related to the onset of ODD, but it may not be causing the disorder as the only significant factor (see Table 1).

2.2. The DRD4 gene

The DRD4 gene controls the passing of neural signals. This gene's polymorphism contains 48-bp Variable Number Tandem Repeat which can affect the function of the dopamine D4 receptor [4]. This suggests that the polymorphism of the DRD4 gene would disrupt the neural signals passing across synapses. This means that emotions and behaviours will be affected, which implies that the DRD4 gene is related to behavioural and emotional control. Koyama et al [4]. identified that the 4 repeat and 7 repeat (7R) alleles of DRD4 gene have a close relationship with psychiatric illness. Research has shown that the 7R is able to reduce the sensitivity of the receptor and results in a decrease in the binding of dopamine [4]. As dopamine is related to happiness and calming emotions, the disruption of the binding up of dopamine results in less dopamine in the system which may lead to negative emotions and ASBs. This implies that the 7R allele of the DRD4 gene may result in ODD. The study of Gadow et al. further supported this conclusion as they found children who carry the 7R allele are reported to show more oppositional behaviours than non-carriers.

However, on the other hand, there is no evidence to show that the DRD4 gene can directly cause APD [10]. Besides, most of the studies rely on the G x E interaction as the cause of ODD, therefore, they fail to provide evidence for the significance of genetic factors only. Additionally, related studies are often small in sample size. The sample is less representative and as a result, the findings cannot be generalised to the larger population of individuals who have psychiatric illness. Thus, this means that the DRD4 gene may not be very significant in causing ODD, which further leads to the conclusion that genetic variables are not significant without the help of environmental variables in the onset of ODD (see Table 1).

2.3. The 5-HTT gene

Another genetic variable that may result in the onset of ODD is the 5-HT transporter (5-HTT) gene. The 5-HTT gene is a serotonin transporter gene. Its 5-HTTLPR polymorphism consists of 22 repeats of nucleotides. There are two common alleles: one is a short (S) allele, and the other is a long (L) allele. The long allele is shown to be associated with aggression among Italian children [4]. They

found further evidence that low SES accompanied with 5-HTTLPR long alleles has a significant effect on ASBs. This suggests that the polymorphism of the 5-HTT gene has a possibility of resulting in defiant disorders due to the tendency of showing aggression, which may lead to ODD among children.

On the other hand, most of the literature failed to find a main significant effect of the 5-HTT gene. This illustrates that the studies of 5-HTT gene lack statistical power to detect the effects of this gene. Addressing this, Koyama et al [4]. found the interaction between different genes may exert a noticeable influence on aggressive behaviours, however, it is strictly in the context of sexual abuse. This suggests that the 5-HTT gene may not be impactful in causing ODD due to the lack of other genes and environmental factors. This means that the onset of ODD is complicated and the interaction of genetic and environmental variables is not negligible (see Table 1).

Table 1. Key genetic factors associated with ODD

Gene	Polymorphism	Functional Impact	Association with ODD	Ref.
MAOA	MAOA-uVNTR	Modulates MAO enzyme activity, affecting 5-HT, NE, and DA metabolism	Low-activity alleles (short allele, 2-repeat allele) associated with oppositional behaviors and aggression	[4, 8, 9]
DRD4	48-bp VNTR	Affects D4 receptor function, altering dopamine signaling	7-repeat allele (7R) reduces receptor sensitivity, linked to oppositional behaviors	[4, 10]
5-HTT	5-HTTLPR	Regulates 5-HT transport, impacting serotonergic system	Long allele (L) interacts with low SES, increasing risk of aggressive behavior	[4]

3. Environmental factors

3.1. Childhood maltreatment

Another well-known factor in causing conduct problems among children is childhood maltreatment. Negative parenting involves neglect and abuse, which means childhood maltreatment can be explained as behaviours that cause damage or potential damage to an individual who is below the age of 18 [11]. The longitudinal study conducted by Degli Esposti et al. shows that childhood maltreatment is associated with ASB at all ages and different types of abuse are related to mental illness at different ages of life [12]. For instance, emotional abuse affects the formation of ASB at all ages except the age of 7 and sexual abuse only affects children's mental state after the age of 16. Moreover, neglect also results in the onset of ASB at the early stage of life, however, the influence of neglect decreases as the age increases as neglect is shown to be related to a steeper rate of change of influence over time. This is solid evidence that childhood maltreatment is related to the onset of ODD as ODD is an example of antisocial behaviours among children. Further evidence would be that physical abuse is shown to have a significant effect on higher levels of ASBs, and it does not change across adulthood. This implies that physical abuse is an important variable to the production of ASB, which further supports that negative parenting is a significant factor in causing ODD among children.

The studies that investigate the effect of childhood maltreatment are reliable and representative. This is because the sample sizes are large, and the categories of childhood maltreatment are covered completely. However, on the contrary, more effort is needed in investigating childhood maltreatment as a factor in causing ODD. For example, the MAOA x Childhood maltreatment interaction shows that kids who have experienced maltreatment and possess the MAOA gene are more likely to display a higher level of ASB. This means that genetic factors may be necessary when analysing the

cause of ODD [3]. Secondly, the aetiology of ODD may be more diverse than being caused only by childhood maltreatment. For example, maternal emotions may also be a factor that contributes to the onset of ODD as mentioned above. Maternal emotions may lead to negative parenting and further result in abuse. This means that other environmental variables are necessary for the development of childhood maltreatment and therefore it cannot be the only reason that causes ODD. Furthermore, Degli Esposti et al. have stated that childhood maltreatment is a risk factor for the early appearance of children's mental disorders [12]. This means that there is no causal relationship between negative parenting and the production of ASB but only a correlational relationship exists. Therefore, childhood maltreatment may not be able to explain the occurrence of ODD as the only factor.

3.2. Socio-economic status (SES)

Another environmental variable that contributes to the onset of ODD is the SES of the family. SES refers to individuals' status in society within the social hierarchy. A combination of social and economic variables is used to measure SES [7]. Evidence from a longitudinal adoption study indicates that children in non-adoptive families from lower SES backgrounds exhibit higher levels of antisocial behaviour [13]. Low SES individuals are seen as poor at making decisions in the area of health and finances. Their residences are unstable, and their educational level is often low. This means that the children raised in such low SES families would have a childhood with changes all the time. This is not beneficial for their education and mental wellbeing, which predisposes them to the development of ODD. Besides, Gresko et al. investigated the Colorado Adoption Project and found that SES in early stage of life is an independent predictor for ASBs. This indicates that SES acts as a risk factor for oppositional defiant behaviors which may contribute to the development of ODD. On the other hand, research shows no significant link between SES and the initial onset of antisocial behavior. Gresko et al. only detected a significant effect of SES during the early childhood stage of development [13]. This finding suggests that SES cannot directly affect antisocial behavior when individuals reach older age groups. Most studies exploring the influence of SES rely on self-report methods which may reduce the overall validity of results. Self-report data lack reliability because participants may alter responses due to social desirability and demand characteristics. Such biases make the findings of these studies less trustworthy for further scientific analysis and interpretation. This uncertainty implies that SES may not actually be a direct cause for the development of ODD in individuals.

4. G x E interaction

Since both factors appear equally important, the G x E interaction provides another explanation for the onset of ODD. This mechanism states that mental disorders arise from a combination of environmental and genetic variables together. It shows that the etiology of ODD is highly complex and cannot be explained by any single factor alone. For instance, the MAOA-S genotype and adverse childhood experiences together contribute to the development of ASB [9]. This finding supports the conclusion that ODD emerges from the interaction between genetic and environmental factors. Increased research on epigenetics has shown that the environment can change the effects of genetic traits in certain conditions [14]. This means that environmental factors can alter how genetic factors influence disorder development in real situations. Genetic factors create a predisposition to ODD, and environmental factors often trigger the actual onset of the disorder. Herrera-Luis et al [2]. investigated the G x E interaction and confirmed that mental disorders have multiple causes. Their study shows that this interaction plays the most critical role in psychological disorders among

children and adolescents. Thus, existing evidence strongly suggests that ODD results from combined genetic and environmental stress influences.

5. Conclusion

The onset of ODD is influenced by predisposing genetic factors. Firstly, the MAOA gene is related to emotional control, which further indicates that the MAOA gene is related to emotional issues such as impulsivity, aggression, and deviant behaviours. This implies that the MAOA gene is influential in causing the onset of ODD among children. Besides, the 7 repeats (7R) allele of the DRD4 gene reduces the sensitivity of the dopamine receptors which decreases the effect of dopamine. This suggests that the DRD4 gene may lead to the occurrence of ASBs. As well as the DRD4 gene, the 5-HTT gene is also shown to be related to ODD. The S allele of the 5-HTTLPR polymorphism predisposes individuals to an increased risk of violent behaviors, which implies that the 5-HTT gene is closely related to antisocial behaviors and thus the onset of ODD. However, environmental factors also play a crucial role in causing ODD. Childhood maltreatment includes various harmful actions such as emotional abuse, physical abuse, and neglect, which damage the psychological and physical health of children and act as key stressors that trigger antisocial behaviors. Furthermore, socioeconomic status (SES) is another factor that may contribute to the development of ODD. Low SES means that individuals often face worse health conditions, lower educational levels, and poor decision-making abilities. Therefore, children raised in low SES families tend to have an unstable childhood due to frequent home relocations, and they are more likely to live in high-risk communities. This unstable environment increases the risk of children developing antisocial behaviors, which in turn leads to a higher chance of developing ODD. In conclusion, genetic factors create a predisposition for the emergence of antisocial behaviors and thus ODD, while environmental factors act as triggers for the onset of this condition. Therefore, the etiology of ODD lies in the interaction between genetic factors and environmental influences.

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