

# Psychiatric Comorbidities in Conduct Disorders and Neurobiological Bases

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## Abstract

Conduct disorder is rarely isolated, and the international literature shows a high and very diverse comorbidity. This article presents in particular the psychiatric comorbidity of conduct disorder with other externalized disorders such as attention deficit hyperactivity disorder (ADHD), oppositional defiant disorder (ODD), and internalized disorders such as mood disorder (depressive and bipolar disorder), anxiety disorders, including post-traumatic stress disorder and substance use disorders (abuse/dependence). These disorders seem to have a neurobiological substrate which implicates brain and hormonal changes, neurotransmitters alterations and environmental influences.

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## Introduction

Conduct disorders represent a diverse spectrum of conditions characterized by disruptive, impulsive, or aggressive behaviours. Conduct disorders, commonly associated with defiant, impulsive, or aggressive behaviours, are an area of significant concern in mental health, especially in children and adolescents. These disorders can have a variety of causes, including genetic, neurobiological, and environmental factors (Nock, M. K., Kazdin, A. E., Hiripi, E., & Kessler, R. C. (2006)). This review provides an overview of conduct disorders, comorbidities, and their underlying underpinnings.

## Definitions of comorbidity

The term "psychiatric comorbidity" means the presence of two or more disorders in the same individual, which is established by systematic clinical evaluation. The phenomenon of psychiatric comorbidity has been analysed in general and clinical populations (Angold et al., 1999).

It should be noted that the first quantitative description in the general population of psychiatric comorbidity in children and adolescents is relatively recent, dating from 1987 (Kashani et al., 1987). Since this study, interest in comorbidity has increased considerably due to the fact that it is not just a combination of disorders defined by a classification system. In fact, a comorbid disorder can have an impact on the symptomatology and future of the disorder under consideration. In addition, many authors insist on the importance and necessity of taking comorbidity into account in understanding the etiology of the disorder and its treatment (Nottelmann and Jensen, 1995; Rutter, 1997).

Psychiatric Comorbidities of conduct disorder can be distinguished from externalized disorders and internalized disorders.

## Comorbidity with other externalized disorders

Among externalized disorders, attention deficit hyperactivity disorder and oppositional defiant disorder are frequently associated with conduct disorder and could be part of the same clinical entity.

### Attention deficit hyperactivity disorder (ADHD)

ADHD is one of the psychiatric pathologies most associated with behavioral disorders and ODD.

Most epidemiological studies explain this co-occurrence by the existence of continuity between ADHD in childhood and conduct disorder in adolescence. This type of data refers to the trampoline model in which ADHD is the first step in progression to conduct disorder, suggesting that these two disorders are part of the same clinical entity. For Rutter (1997), these two disorders could reflect different phases of clinical manifestations of the same subsyndromic inclination. It would be a successive comorbidity explained by processes common to these two disorders. According to Biederman et al. (1996), ADHD in childhood is more predictive of conduct disorder if it is associated with ODD.

However, recent analyses of data from 6 longitudinal studies (Nagin and Tremblay, 1999; Broidy et al., 2003) in 3 different countries (Canada, New Zealand, United States), as well as work on the development of symptoms of these different disorders in early childhood, indicate that ADHD and conduct disorder appear at the same time during the second year of life. Therefore, it would often be a competitive comorbidity.

Several characteristics were associated with the subgroup of children with both disorders. The comorbidity between these two types of disorder is associated with relational difficulties (rejection of peers, lack of close friends, dysfunctional interactions with parents...), academic (schooling) and social difficulties such as delinquent behavior, difficulties that are much greater in these children (Fletcher et al., 1996; Kuhne et al., 1997; Satterfield and Schell, 1997; Gresham et al., 1998) and increase over time (Gresham et al., 1998). Children with this comorbidity are reported to have more antisocial and illegal behavior during adolescence and are more likely to be incarcerated (Mannuzza et al., 1991; Lynam, 1996; Soderstrom et al., 2004). All of these problems may be associated with more severe symptoms than isolated conduct disorder (Hinshaw et al., 1993; Kuhne et al. 1997). For Lynam (1996), the clinical profile that associates hyperactivity, impulsivity and attentional difficulties with conduct disorder would be characterized by high levels of aggression and

criminal violence.

In summary, it appears that the comorbidity of conduct disorder with ADHD is often associated with increased symptomatology in each of the disorders.

### Oppositional defiant disorder (ODD)

Some authors (Kuhne et al., 1997) and classifications (ICD-10) return to ODD with conduct disorder in the same generic category (disruptive disorders, disruptive conduct disorders). Others, on the other hand, advocate a distinction between these two disorders to the extent that not all children with ODD have or will present a conduct disorder (Biederman et al., 1996; Greene et al., 2002).

The study by Greene et al. (2002) examined the associations between ODD and conduct disorder. Drawing from 1,600 10-year-olds and divided into three groups: a group with TOP (N=643), a second group with conduct disorder (N=262) and a third group with TOP and conduct disorder (N=675). The results showed that of all children with ODD, only 27.7% had conduct disorder. In addition, the group of children with ODD was characterized by a higher level of psychiatric comorbidity (bipolar disorder, ADHD, depressive disorders, and anxiety disorders) and greater social and family dysfunction than other populations. As with ADHD, it appears that this group combining conduct disorder and ODD may constitute a specific subgroup with a unique developmental trajectory (Loeber et al., 1994). According to Fergusson et al. (1996) and Loeber et al. (1994 and 1998), this clinical profile of conduct disorder is a prodromal form of antisocial personality disorder in adults. TOP as a precursor disorder of conduct disorder would be identified as the early marker of a process launched very early that increases over time, which can lead to the installation of a pathological personality.

Ultimately, it appears that comorbidity with ODD, whether concurrent or sequential, aggravates the severity of conduct disorder symptomatology (Broidy et al., 2003).

## Comorbidity with internalized disorders

In this part, we will distinguish mood disorders that combine depressive disorder and bipolar disorder, and anxiety disorders with special attention to post-traumatic stress disorder (PTSD).

### Mood disorders

The association of depression with conduct disorder or ODD is strong (Angold et al., 1999). For some authors, this comorbidity is the consequence of a bidirectional action of these two disorders, each of the disorders involved in the onset and maintenance of the other (Quiggle et al., 1992; Fergusson et al., 1996). For example, subjects with a behavioral disorder will present behavioral and emotional difficulties with harmful effects at the academic and social level, and all negative social responses (sanctions, punishments...) returned to these children will induce negative effects (depressive cognitions), persecutive experiences that will reinforce relational difficulties and antisocial behaviours. On the other hand,

the association of conduct disorder with depressive disorder would increase the risk of suicide.

The combination of conduct disorder and depression would be a vector of susceptibility to suicide, especially when associated with alcohol consumption (Brent et al., 1993; Lewinsohn et al., 1994). Shaffer et al. (1996) would later develop the triple pattern model (comprising conduct disorder, depression, and substance abuse) as being at risk for suicidal action. In this model, depressive comorbidity would play an important role. However, this model is contradictory and a study (Renaud et al., 1999) conducted on a small sample of 55 suicidal adolescents with disruptive disorders (ADHD and conduct disorder) results in a moderating effect of depressive disorder on the transition to suicidal act. Finally, the study of the links between conduct disorder and depressive disorder argues in favor of bidirectional comorbidity.

The second mood disorder comorbid to conduct disorder is bipolar disorder (BPD). Studies have studied rates of conduct disorder ranging from 16.9% to 42% (Kovacs & Pollock, 1995; Biederman et al., 1999; Masi et al., 2003; Wozniak et al., 2004). For some authors, it is a successive comorbidity in which bipolar disorder is present during childhood and predisposes to the onset of conduct disorder (Kovacs and Pollock, 1995; Masi et al., 2003). The extreme severity of juvenile mania, due to its behavioral and emotional symptoms, would predispose to conduct disorder. Wozniak et al. (1995) even suggest that the symptomatology of bipolar disorder can be interpreted as conduct disorder. Bipolar children with severe behavior problems, such as theft, vandalism, and dropping out of school, may be diagnosed with conduct disorder. The question of chronology remains open, since these two problems can appear simultaneously during childhood (Biederman et al.; 1999). These forms are most often "familial" with the presence of conduct disorder in siblings and antisocial personality disorders in parents (Wozniak et al., 2001).

Comorbidity is thought to increase conduct disorder symptomatology with higher levels of aggression and hostility, promote antisocial personality mating in adulthood, and increase the risk of dependence on alcohol and other psychoactive substances (Biederman et al., 1997).

### Anxiety disorders

General population data indicate a high comorbidity of conduct disorder with anxiety disorders (Angold et al., 1999). In general, studies (Walker et al., 1991) highlight a moderating effect of anxiety disorders on the severity of conduct disorder in the general and clinical population, as well as on antisocial functioning (decreased risk of school failure, relationship dysfunction, contact with police, use of psychoactive substances). In the long term, this comorbidity would also have a protective effect against the pairing of an antisocial personality in adulthood. On the other hand, this effect seems to be less present in severe forms of conduct disorder, especially those found in the prison population. In their study of incarcerated adolescents, Ollendick et al. (1999) found that the presence of an anxiety disorder had no effect on the severity of conduct disorder symptomatology, the number of antisocial behaviours, and the age of first manifestations.

One of the most comorbid anxiety disorders for conduct disorder is post-traumatic stress disorder (PTSD) (Cauffman et al., 1998; Reebye et al., 2000). Within this comorbidity, there is a clear gender effect, with girls with conduct disorder more likely to develop PTSD than boys (Reebye et al., 2000). Symptoms appear more severe for girls than for boys (anhedonia, sleep disorders, attention difficulties) (Lipschitz et al., 1999; Reebye et al., 2000). This difference between girls and boys

is thought to stem from the nature of the trauma experienced: girls experience more sexual violence, while boys are mostly victims of physical assault, accidents, or deaths. This comorbidity appears to be even higher in severe forms of conduct disorder (e.g., in prison populations) where the rate of comorbidity is approximately twice that in adolescents in the general population (Steiner et al., 1997; Cauffman et al., 1998). Thus, it appears that while the existence of PTSD increases the risk of conduct disorder, conduct disorder itself is at risk for the onset of PTSD, as adolescents with PTSD are more exposed to trauma-prone situations.

### Substance use disorders (tobacco, alcohol, drugs)

Among the psychiatric disorders often associated with substance use, conduct disorder ranks prominently. Many studies have highlighted a high comorbidity in adolescence between conduct disorder and alcohol and illicit substance abuse (Fergusson et al., 1993; Hovens et al., 1994; Disney et al., 1999; Flory and Lynam, 2003). Depending on the study, the prevalence rate varies between 32% and 96% of cases. Gender appears to play a role in the clinical expression of this comorbidity. In fact, adolescent girls are characterized more by depressive or even anxious symptomatology, while boys have essentially violent and criminal symptomatology (Riggs et al., 1995; Simkin, 2002).

Some longitudinal studies have shown that psychological substance abuse is secondary to conduct disorder. Conduct disorder appears to be the psychopathological disorder that is most predictive of alcohol, drug, and tobacco abuse/dependence (Disney et al., 1999). In general, the precocity and severity of this disorder play a decisive role in the initiation and maintenance of abusive behavior (Crowley et al., 1998; Myers et al., 1998; Pedersen et al., 2001). The risk of comorbidity would be higher for early-onset behavioral disorders (conduct disorder, ADHD, ODD) (Ridenour et al., 2002). In addition, the emergence of an antisocial personality is thought to be promoted by the severity of conduct disorder and substance abuse (Crowley et al., 1998; Fischer et al., 2002).

With respect to cannabis use, conduct disorder is predictive of early onset (Fergusson et al., 1993). This bond would be stronger for girls than for boys.

For tobacco, conduct disorder is primarily predictive of heavy tobacco dependence (Breslau, 1995; Brown et al., 1996; Riggs et al., 1999; Upadhyaya et al., 2002). The predictive link is even stronger when conduct disorder is comorbid with ADHD. This combination would predict early initiation of tobacco, high physical dependence on nicotine, as well as greater difficulties in quitting smoking (Breslau, 1995; Riggs et al., 1999).

Early initiation of psychoactive substances is also thought to play an important role in the severity of conduct disorder and the persistence of antisocial behavior (Robins and Prysbeck, 1985; Myers et al., 1998). In fact, substance use disorders increase delinquency problems and emotional difficulties.

All the studies point to a bidirectional influence of the two types of disorders (Caspi et al., 1989; Moffitt, 1993). Moffitt (1993) explains this phenomenon (concurrent comorbidity between conduct disorder and substance abuse). According to this author, young people who adopt deviant behaviours will develop dysphoria related to their social crimes and will self-medicate, in a way, by taking psychoactive substances. In addition, the behavioral and emotional consequences of

substance abuse will limit the subject chances of escaping an antisocial lifestyle. Thus, this high comorbidity would be the expression of a cumulative continuity described by Caspi et al. (1989): addictive behaviors that favor criminal behaviors and criminal behaviors that involve the use of illicit substances.

Among other comorbid externalized disorders, the association of conduct disorder and ADHD appears to be more conducive to substance psychoactive disorders (Molina et al., 2002). Some studies support this (Mannuzza et al., 1991; Claude and Firestone, 1995; Chilcoat and Breslau, 1999). This association has been primarily related to the severity of dependence in adolescents followed by substance abuse/dependence (Thompson et al., 1996; Molina et al., 2002). However, other authors have not confirmed this link (Disney et al., 1999).

In addition, some authors suggest combinations of comorbidity between depression, anxiety, conduct disorder and substance use in adolescence (Babor et al., 1992; Neighbors et al., 1992; Hovens et al., 1994). The study by Neighbors et al. (1992) in the context of incarcerated adolescents shows that substance abuse (alcohol and cannabis) is associated with conduct disorder in almost all cases, as well as a strong co-occurrence of depressive disorders and conduct disorder with substance abuse and poly-substance use. Therefore, in this population, substance abuse is strongly related to conduct disorder, especially when depression is associated with it. The appearance of a depressive or anxiety disorder during the course of conduct disorder would constitute, according to the authors, a precipitant factor in the abuse of psychoactive substances.

Finally, comorbidity between conduct disorder and psychoactive substance abuse is very common, insofar as criminal behaviours predict the use of psychoactive substances and the addictive process promotes antisocial behavior.

## Neurobiological basis

### Brain structure and function

Conduct disorders have been associated with alterations in various regions of the brain. The prefrontal cortex, responsible for regulating behavior and decision-making, is one of the most researched. It has been observed that individuals with conduct disorders may have a less active or developed prefrontal cortex, which could influence impulsive or aggressive behaviours (Raine et al., 1997). In addition, alterations in the limbic system and basal ganglia may also be linked to these disorders.

### Neurotransmitters

Alterations in the balance of neurotransmitters are key in the development and manifestation of behavioral disorders. Reduced serotonin levels have been observed to be associated with impulsivity and aggression (Kruesi et al., 1990). Dopamine and noradrenaline also play crucial roles in modulating behavior and their alterations may be linked to behavioral disorders.

## Genetics

Studies of twins and families suggest that there is a genetic predisposition to develop conduct disorders (Moffitt, 2005). Although several genes may be involved, the interaction between genetic and environmental factors is essential for the manifestation of the disorder.

## Environmental influences

Traumatic experiences, abuse, and neglect can interact with genetic predispositions and trigger behavioral disorders (Teicher et al., 2003). These experiences can cause neurobiological changes, including structural and functional alterations in the brain.

## HPA axis deregulation

The hypothalamic-pituitary-adrenal (HPA) axis regulates the stress response.

Dysregulation in this system has been associated with conduct disorders, suggesting that the stress response may be a determining factor in the onset and severity of the disorder (Popma et al., 2007).

## Conclusion

The international literature highlights an important comorbidity in conduct disorder, psychiatric comorbidity with other externalized disorders (ADHD), internalized disorders (mood disorders, anxiety disorders), disorders related to the use of psychoactive substances (alcohol, tobacco, drugs). In general, the association of conduct disorder with ADHD, ODD or bipolar disorder increases the severity of the symptomatology in each of the disorders. On the other hand, the presence of an anxiety disorder would have a moderating effect on conduct disorder, but long-term detrimental consequences. It was also noted that conduct disorder could be at risk of onset of post-traumatic stress disorder, and vice versa. Thus, beyond this clinical description, the analysis of comorbidity allows to highlight clinical subgroups that can be heuristic both for the etiological understanding and for the study of the evolution of the conduct disorder. Finally, examination of behaviours associated with conduct disorder also reveals that conduct disorder is strongly related to different risky behavioral behaviours (e.g., road hazards, sexual risks, etc.). Finally, los trastornos de conducta son condiciones complejas que requieren un enfoque multifacético para su diagnóstico y tratamiento. Comprender sus bases neurobiológicas y factores contribuyentes puede ayudar en el desarrollo de tratamientos más efectivos.

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