



UNDERSTANDING SEX-BASED DIFFERENCES IN CHILDHOOD CONDUCT DISORDER

SARAH ALLAM*[1], ROOHI DEVJE*[1], LINDA DUONG*[1], NIMRA HOODA*[1], SAMANTHA RUTHERFORD*[1]

[1] BACHELOR OF HEALTH SCIENCES (HONOURS), CHILD HEALTH SPECIALIZATION, CLASS OF 2025, MCMASTER UNIVERSITY
*ALL AUTHORS CONTRIBUTED EQUALLY

ABSTRACT

Externalizing symptoms are behaviours that violate major social norms, such as aggression, violation of rules, or deceitfulness. Conduct disorder (CD) is a mental disorder defined by patterns of externalizing behaviour. Recent studies find a significant discrepancy in the rates of childhood diagnosis between sexes, with a higher prevalence for boys compared to girls. Consequently, it has been suggested that current diagnostic criteria may not fully capture the nuanced manifestation of CD in girls. This paper aims to explore theories of sex differences in CD and implications for diagnostic criteria as described in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-5-TR). Through a review of the literature, this study examines childhood sex-specific differences in the symptoms, subtypes, comorbidities, and neurobiological correlates of CD. Theories discussed include the gender paradox, delayed onset pathway, and familial perspective theories. Based on sex-specific findings, implications for screening and diagnosis are discussed. In addition, the suggestion of advocating for further research on modifications in DSM criteria and use of sex-specific risk assessment tools is included. Research in this area has the potential to challenge misconceptions surrounding sex, gender, and externalizing behaviour with the goal of improving outcomes for Canadian youth with CD.

INTRODUCTION

According to the American Psychiatric Association, conduct disorder (CD) is a mental disorder characterized by self- and informant-reported continuous externalizing behaviour patterns that violate major age-appropriate social norms and rules, as well as rights of others [1]. This is in contrast to internalizing symptoms, which constitute internal anxiety and mood disorders, for

example. The externalizing behaviours typical of CD—which can emerge in early childhood or adolescence—are grouped into four categories in Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-5-TR): aggressive conduct that causes or threatens physical harm to other people or animals, nonaggressive conduct that causes property loss or damage, deceitfulness or theft, and serious violations of rules. Children with CD may also receive the specifier “with limited prosocial emotions” for exhibiting a lack of remorse or guilt, callous-unemotional (CU) traits, being unconcerned with performance, or shallow affect.¹ Children with CD may also receive the specifier “with limited prosocial emotions” for exhibiting a lack of remorse or guilt, callous-unemotional (CU) traits, being unconcerned with performance, or shallow affect [1].

Prevalence estimates of CD vary, ranging from 2-10% globally [1]. A recent review reported that the pooled global prevalence of CD is 3.0%, with boys being 2.6 times more likely to be diagnosed compared to girls [2]. In Ontario, recent estimates from the Ontario Child Health Study suggest that in children aged 12-16, the prevalence of CD is 2.52%, with higher estimates for boys (3.08%) than girls (1.92%) [3]. Taken together, these data illustrate the sex-based differences in the diagnosis of CD. Some authors have noted that the diagnostic criteria of the DSM-5-TR is not reflective of CD as it presents in women and girls [4].

The purpose of this paper is to explore theories as to why sex differences exist, synthesizing recent findings on differences in the symptoms, subtypes, comorbidities, and neurobiological correlates of CD, and discussing implications of these findings for current diagnostic procedures in Canada using the DSM-5-TR and early screening methods. This research recognizes that there are construct differences in sex and gender, and that various studies may assess different aspects of identity. Throughout this article, “male” and “female”, “girls”

and “boys” are used interchangeably to refer to the sex of the individual. The conflated constructs of sex and gender in psychological research is a limitation that must be acknowledged, and all evidence should be considered with the knowledge that nuances of socially-conceptualized gender and individuals beyond the binary are not captured [5].

RESEARCH QUESTION

How can DSM diagnostic procedures and early screening methods be adjusted to consider potential sex differences in Canadian children and youth with CD?

To answer this research question, we will investigate the following:

1. Are there sex differences in the symptoms, subtypes, comorbidities, and neurobiological correlates of CD?
2. What are the major hypotheses that account for these sex differences?
3. To what extent do current DSM diagnostic procedures and early screening methods account for sex differences in CD?

RATIONALE

Sex differences in the manifestation of CD is an emerging topic in research; however, established knowledge and current literature has several limitations. Far less is known about the causes of CD in females due to the majority of early mechanistic studies being restricted to male patients [6]. Furthermore, an insufficient number of female subjects have been included in research examining the sex differences in such antisocial behaviour despite it recently being established that there are epidemiological differences in prevalence [6]. There are conflicting theories surrounding these sex differences and the neurodevelopmental origins of CD [6]. The evidence surrounding current theories should be considered, considering its potential implications for current diagnostic and classification systems. Progress in this area can work to dismantle stereotypes surrounding sex, gender and externalizing behaviour, fostering more nuanced approaches to assessment and treatment, and preventing the underdiagnosis of children who may benefit from care [7].

METHODS

This paper primarily uses evidence from recent peer-reviewed journal articles and sources located on Google Scholar, Web of Science, PsychINFO, and PubMed/Medline. The table below describes the keywords employed.

| Search Topic | Conduct Disorder | | Sex Differences | | Diagnosis |
|--------------|--|-----|--|-----|---|
| Search Terms | "conduct disorder*" OR CD OR "externaliz* disorder*" | AND | male OR female OR girl* OR boy* OR woman OR women OR "man" OR "men" OR gender* OR sex* | AND | diagnos* |
| | | | | | Presentation |
| | | | | | symptom* OR presentation* or manifestation* |

In addition to traditional database searches, forward and backward citation searches were also conducted on identified articles.

Evidence was limited to English and French publications. Given the little amount of literature in this area, there was no limitation on the type of study. Further, any study discussing externalizing disorders in general was included if there was an explicit mention of CD as one of the conditions studied.

Data was synthesized in a qualitative manner.

DIFFERENCES IN THE CLINICAL MANIFESTATIONS OF CONDUCT DISORDER ACROSS GENDERS

Theories

There are several theories that seek to explain and describe gender differences in the clinical manifestation of CD, many of them still pending investigation.

Gender Paradox and Differential Threshold:

The gender paradox theory refers to the fact that although the prevalence of girls with CD is lower than boys, girls typically present with more severe behaviour problems and more co-occurring symptoms and disorders [8]. Related to this concept is the differential threshold of female CD theory, which suggests that the current diagnostic criteria for CD are not sensitive to the nuances in female presentation [1,9].

Delayed Onset Pathway:

The delayed onset pathway theory claims that the onset of CD in girls is usually during adolescence (AOCD), and thus typically later than boys who have an average childhood onset of CD (COCD) [10].

Familial Perspective:

Finally, one ongoing discussion is the familial perspective [11]. One review exploring family functioning and processes and associations with CD, found that one possible explanation for sex differences in CD presentation is that parents tend to emphasize prosocial behaviours and control of anger in girls, treating them with less aggression and more warmth compared to boys [11]. Girls are also more closely monitored by parents, potentially acting as a protective factor against disruptive behaviour. However, in girls who display a high number of externalizing behaviours, reciprocal associations between child disruptive behaviour and parenting behaviour explains why symptoms may be more severe in girls; this is the idea

that the child's temperament and caregiver's behavioural responses feed into each other, and over time, both reinforce and worsen the externalizing behaviours [11]. Additionally, with regards to adolescent-onset disruptive behaviour, there may be a risk period during puberty for girls. Parental monitoring decreases during this transition, which is related to an increase in interpersonal conflicts and externalizing behaviour. Girls' friendships, characterized by greater intimacy, may influence their behaviour, and involvement with deviant peers might be more negative for girls than boys.

Comorbidities

The DSM-5-TR outlines various comorbidities and complications of CD that span from childhood to adulthood. These include learning disabilities, diminished academic achievement, attention-deficit/hyperactivity disorder (ADHD), mood disorders, anxiety disorders, psychotic disorders, somatic symptom disorders, impulse-control disorders, and post-traumatic stress disorder (PTSD) [1,12]. Children diagnosed with CD may progress into adulthood with an elevated likelihood of developing antisocial personality disorders [13]. Furthermore, the DSM-5-TR states that behavioural challenges associated with the disorder may result in children and youth with CD encountering issues related to substance use and criminal convictions [1]. Individuals with CD also face an elevated risk of suicidality and poor life satisfaction [1]. It is noted that CD is associated with higher rates of suicide attempts even after adjustment for comorbid mood, anxiety, and substance use disorders [1]. It is worth noting that the DSM outlines differences across genders in CD comorbidities, specifically when it comes to substance use. While the association between CD and substance use is well-established, higher rates are observed in adolescent females [1]. The reason behind this gender difference is theorized to be due to females reaching puberty at an earlier age than males [14]. The 2006 Minnesota Twin Family Study suggests that genetic influences on CD are moderated by the timing of menarche in girls. Early puberty/menarche in girls has been linked to higher rates of CD symptoms, an earlier initiation of the disorder, greater frequency of substance use, and earlier sexual activity [14]. In contrast, girls with delayed menarche appear to be protected from the well-documented increase in externalizing behaviour during adolescence [14]. As puberty in boys and girls involves different social and biological phenomena, it remains unclear whether these findings would generalize to boys, and future research should seek to evaluate the impact of early pubertal timing on CD longitudinally in boys [14].

There is evidence that females with CD are also more likely to have comorbid externalizing and internalizing disorders compared to their male counterparts, who generally display heightened rates of externalizing disorders alone [15]. Furthermore, early depressive symptoms are a stronger risk factor for delinquent behaviour in females than in males. It was found that girls exhibit both delinquency as a predictor for

subsequent depression and depression as a predictor for increased subsequent delinquency. In males, only early delinquency predicted subsequent depression across adolescence [15].

Further, females with CD are more likely to exhibit comorbid depression than males, a finding consistent with the gender paradox hypothesis [16].

Timing Differences

Research indicates that childhood onset of CD is less common in girls than in boys, with a higher prevalence of onset during adolescence [17]. Only 1-2% of girls follow the childhood onset trajectory of CD, compared to 5-10% of boys. Sex difference ratios ranging between 10-15:1 for boys to girls with CD have been reported [18-20]. It is important to note only 1-2% of females from population-based or birth cohort samples were followed from childhood through adulthood, complicating prevalence estimates. This is a significant gap because childhood onset conduct disorder (COCD) has been associated with serious adjustment and antisocial problems in young adulthood, suggesting that young girls with COCD may be underdiagnosed and lack necessary support relative to other subtypes [21]. Despite an influential model describing two distinct trajectories of CD onset and the observation of increased adolescent onset conduct disorder (AOCD) in girls, these girls tend to resemble COCD boys on personality traits, such as poor impulse control and callous-unemotional (CU) traits [22]. This highlights that CU trait symptomatology may not be as uncommon in AOCD in girls and may not be restricted to COCD.

Behavioural/Symptomatic Differences

Beyond differences in comorbidities and diagnostic timing, there are several differences in the symptoms of CD presented by girls compared to boys. A recent preliminary study found that males with CD made significantly more risky choices than male controls, while females did not differ significantly from their typical female counterparts regarding such risk- and reward-seeking behaviours [23]. This finding suggests that sex differences exist in reward-related decision-making for youth with CD and that these differences are more pronounced in males with CD. These differences in risk-taking behaviour may also relate to the earlier discussion of internalizing versus externalizing symptoms in boys versus girls. Girls with CD are more likely to have comorbid internalizing disorders compared to their male counterparts, who generally display heightened rates of externalizing characteristics alone [15].

Regarding physical aggression, while boys in community samples exhibit more physical aggression than girls, clinical samples reveal that both girls and boys with highly impaired CD show equally high levels of physical aggression [15]. This unexplained discrepancy in findings underscores the need for further research to establish the prevalence of physical aggression in females with CD.

However, Females with CD also show higher relational aggression scores than males [24]. The established research indicating that females with CD are more likely to engage in relational aggression has significant clinical implications [25]. For example, callous-unemotional (CU) traits and low affective empathy have been positively correlated with relational aggression and antisocial behaviour [24]. Even after controlling for more severe and early-onset conduct symptoms, children and youth with CU traits exhibit more antisocial symptoms in adulthood, such as adult arrests and antisocial personality symptoms, than those without [26,27]. Furthermore, in females, cognitive empathy is negatively associated with relational aggression [24]. Currently, research has predominantly focused on male-related CU traits; however, girls remain an understudied group in the examination of these traits, which evidently has implications for behaviour and delinquency [28, 29].

Studies have shown that gender differences do exist in the association between CD and risky sexual behaviour. The association is stronger in female youth, with research finding that female juvenile offenders report a higher likelihood of risky sexual behaviour including being less likely to use condoms and having higher rates of STIs than males [30,31]. This underscores the need for gender-specific interventions and preventative supports for youth with CD.

Research has shown that boys exhibit more overt conduct problems such as status and property offenses, while girls are more prone to covert conduct problems such as shoplifting and fraud [32,33]. The lower rates of CD diagnosis in females may potentially be due to underdiagnosis and a lack of recognition of these covert problems which are often less identified. Conflicting evidence has been presented, showing that the gap between male and female rates of delinquent behaviour has narrowed over the last few decades. In particular, violent crimes may predict a greater incidence of CD diagnoses for girls [34]. This highlights the importance of further sex and gender-specific research in this field and underscores its clinical significance.

Research has found that aggressive boys with CD demonstrate reduced autonomic functioning, while aggressive girls with conduct problems exhibit greater functioning. This suggests that there may be different etiological mechanisms underlying psychopathy in males and females [35]. However, limitations to this research have been highlighted due to the overwhelming proportion of male to female participants in most studies, making it difficult to draw definitive conclusions about autonomic activity in both genders.

Another difference that has been highlighted in research involves emotion processing skills, which can act as a framework for explaining the sex differences in CD [36]. Research has shown that girls mostly outperform boys on scales of social cognition, which encompasses emotional processing tasks due to earlier maturation of brain

systems involved in emotional responsibility and regulation [36]. Due to displaying these greater emotional functioning skills, they appear to be better equipped for challenges involving socialization. Furthermore, traditional gender roles do encourage more prosocial behaviour in girls, which may lead to the difference in presentation and manifestation of symptoms of CD.

Neurobiological Differences

There are several neurological and biological differences that may also help explain the differences in CD presentation.

One study using diffusion MRI to examine differences in white matter integrity in children with CD found that abnormalities of the superior longitudinal fasciculus were positively correlated with levels of CD symptoms, which has previously been associated with cognitive deficits in children [37]. Further, the uncinate fasciculus (UF) has a role linking the amygdala and the ventromedial prefrontal cortex; this study found that reduced radial diffusivity in the left UF correlated with increased CD symptoms, especially in girls. This article concluded that abnormalities in brain structure may contribute to the emergence of CD in childhood, playing a particularly important role in girls. CD was associated with cortical thinning and higher gyrification in the ventromedial prefrontal cortex in both sexes. Males with CD showed lower, and females with CD showed higher, supramarginal gyrus cortical thickness compared with controls. Relative to controls, males with CD showed higher gyrification and surface area in superior frontal gyrus, whereas the opposite pattern was seen in females [36].

There are various studies that have investigated differences in the genetic basis of CD. One particular gene of interest is the gene that produces monoamine oxidase-A (MAO-A), an enzyme that catalyzes the breakdown of monoamine neurotransmitters (serotonin, dopamine, and norepinephrine) [38]. This gene, MAO-A is located on the X-chromosome and makes male carriers hemizygous and more at risk to consequences of mutations and other variants. A recent meta-analysis confirmed that high expression variants of MAO-O could increase the risk for antisocial behaviour [38].

Various studies have explored sex hormones as a potential mechanism behind the development of CD. Testosterone and dehydroepiandrosterone (DHEA, the precursor of testosterone) have been suggested to be positively correlated with aggressive behaviour across genders, but particularly male adolescents [39]. The implications of this are not yet known, however, girls with CD have been found to have lower cortisol to DHEA ratios, higher levels of free testosterone, and lower levels of SHBG, indicating a possible hormonal imbalance [40].

This initial evidence that the pathophysiological basis of

CD may be partly sex-specific highlights the need to consider sex in future studies and suggests that males and females may require different treatments, as current physiological treatments (i.e., pharmaceutical agents) are not sex-informed and limited to treating individual symptoms rather than the disorder as a whole.

IMPLICATIONS FOR DIAGNOSTIC PROCEDURES

Rationale for Considering and Modifying the Female-Specific Diagnostic Protocols

The underlying reason for the lower prevalence of CD among females remains unknown [4]. Hypotheses include true sex-related differences in CD, a sex bias against females in the diagnostic criteria; however, both hypotheses are likely to contribute to the overall lower prevalence.

The DSM-5-TR partially includes clinical manifestations in girls. Gender-typical behaviours, including running away, oppositional behaviour, and non-confrontational aggression, are mentioned as typical manifestations in girls with CD. However, the DSM-5-TR does not include gender-specific criteria, and the diagnostic criteria are developed from studies with primarily male samples [1]. Criteria centered around behaviours more common in boys may fail to accurately diagnose CD in girls [5]. Ambiguity regarding the sensitivity and specificity of the diagnostic criteria has raised concerns among clinicians about diagnosis and treatment in female patients.

In order to better account for sex differences in CD presentation among females, several changes to the DSM-5-TR have been suggested [41-46]. The current reliance on criteria developed and validated primarily on boys may contribute to underdiagnosis or misdiagnosis in girls. Three proposed changes to the DSM for CD are discussed below. All three have mixed evidence on their specificity and sensitivity for CD diagnosis in girls and require more research before incorporation into future versions of the DSM.

Firstly, the DSM could incorporate gender-typical behaviours associated with CD in girls. Girls may express relational aggression, defined as hurting others through their social position, more often than boys with conduct problems [41]. It has been proposed that criteria for relational aggression be added to the DSM [5]. However, there is mixed evidence on the overlap between high relational aggression scores and meeting the threshold for CD in girls [42]. More research is needed to examine the validity of this symptom for CD diagnosis.

Secondly, it has been proposed that the symptom threshold for CD in girls be changed from three to two [43]. There is mixed evidence to support this threshold change, with some studies reporting increased sensitivity in diagnosis without a loss in specificity [43], while

some report that the loss of impairment in girls with three symptoms is much higher than those with only two symptoms, thereby not supporting a change in diagnosis threshold [42].

Finally, it has been proposed that the age subsets of CD should be changed for girls; the childhood-onset may not be needed, or the adolescent-onset should be defined as the “absence of any criteria prior to age 13” rather than age 10 [44]. However, there are mixed findings on whether girls with CD truly have a later age of onset [9,44], or if their symptoms become more intense with age but have a similar onset age as boys [42,45,46]. This highlights a need for further research following females from birth to adulthood to establish and confirm the proportion of females experiencing a childhood-onset trajectory. Furthermore, it highlights that modifications and alternatives to the two-trajectory model may be needed to support the observations in development of CD in girls.

Evaluation of the Early Assessment Risk List Version 3 (EARL-V3)

In addition to changing diagnostic procedures, increasing early screening of girls displaying symptoms of CD can help improve detection of CD. The EARL-V3 is one such screening tool that should be rigorously evaluated. The EARL-V3 is a structured professional judgement instrument for children ages 6-12 showing antisocial behaviour that is designed to specifically take a gender-sensitive approach to risk assessment [47]. It has been shown to have moderate-to-high interrater reliability and concurrent validity with other scales that predict rule-breaking and aggressive behaviour [48]. The EARL-V3 should be further validated using longitudinal studies with diverse cohorts of girls, including those with conduct problems and those without, to ascertain its effectiveness in distinguishing between normative behaviours and early signs of CD in girls. As the tool is relatively new, having been released in 2021, more studies are needed to validate it although initial results are promising.

CONCLUSION

In conclusion, addressing the lower prevalence of CD among girls requires a multifaceted approach. Further research, including longitudinal studies and comprehensive assessments of gender-specific symptoms, is imperative to enhance the understanding of CD in girls and improve diagnostic accuracy for better long-term prognosis. Proposed modifications for the DSM-5-TR can encompass gender-specific diagnostic criteria, particularly focusing on adolescent-onset subtypes for girls. Additionally, the evaluation of gender-specific risk assessment tools, like EARL-21G and EARL-20B, is crucial to ensure their reliability and validity in screening for CD outcomes.

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