Sex differences in child-onset, life-course-persistent conduct disorder. A review of biological influences

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Abstract

Sex is widely acknowledged to be an important factor in understanding many aspects of behavior, not the least of which is antisocial behavior. When antisocial behavior manifests itself in the domain of juvenile psychopathology, it often takes the form of a type of conduct disorder (CD) that begins in childhood and is life-course-persistent. There is an overwhelming consensus that there is a massive male preponderance in this type of CD and that biological variables are major influences on this difference. This review built on this consensual scaffolding in an attempt to provide some useful leads for identifying the biological contributions to the predominantly male complexion of life-course-persistent CD by linking it to three different levels of biological mechanisms.

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Sex is widely acknowledged to be an important factor in understanding many aspects of behavior (Stewart & McDermott, 2004). Indeed, as Thomas Insel, head of National Institute of Mental Health recently observed with regard to mental disorders: “It’s pretty difficult to find any single factor that’s more predictive for some of these disorders than gender” (Holden, 2005, p. 1574). The validity of Insel’s observation has no better illustration than conduct disorder (CD).

In the broad spectrum of conduct problems, CD captures the violent, overtly-destructive dimension (McMahon & Frick, 2005) that is codified in Diagnostic and Statistical Manual of Mental Disorders (4th ed., text rev. [DSM-IV-TR]; American Psychiatric Association, 2000). CD refers to the more severe antisocial and aggressive behaviors that result in serious violations of others’ rights (McMahon & Frick, 2005) and its very nature involves aggressive, violent, confrontational behavior (Hartung & Widiger, 1998). Its importance is underscored by the fact that the chronic, severe conduct problems captured by the DSM-IV-TR rubric of CD are the most common childhood difficulties both in the community and in referrals to child mental health facilities in the United States (Dodge & Pettit, 2003; Hill, 2002).
The most widely accepted developmental taxonomy of CD is that which distinguishes between life-course-persistent versus adolescent-limited antisocial behavior (McMahon & Frick, 2005; Moffitt, 2006; Rutter, Kim-Cohen, & Maughan, 2006). Life-course-persistent refers to the childhood-onset of severe conduct problems (i.e., before age 10) which emerge from early neurodevelopmental and family adversity risk factors, tends to be life-course-persistent, and hence is almost always a prognosticator of poor adult adjustment (Moffitt, 2003, 2006). Life-course-persistent individuals in contrast to the adolescent-limited are “...few, persistent and pathological” (Moffitt, 2006, p. 571). However it is precisely these few individuals and families (10%) who commit more than 50% of crimes in the United States (Moffitt, 2005). Hence the importance of understanding the life-course-persistent type, i.e., the “few, persistent and pathological” can hardly be overstated. Note that for the purposes of this review the designation CD will refer to this type.

Apropos of Insel’s observation, boys are about two to four times more likely than girls to develop a form of CD (Dodge, Coie, & Lynam, 2006; Earls & Mezzacappa, 2002; Emé & Kavanaugh, 1995; Loeber, Burke, Lahey, Winters, & Zera, 2000) and, astoundingly, 10 to 15 times more likely than girls to develop the life-course-persistent type (Moffitt, 2003, 2006; Moffitt, Caspi, Rutter, & Silva, 2001), thus prompting Moffitt (2006) to view it as almost exclusively a male phenomenon. This huge sex difference, which is real and not due to any methodological issues of sampling, measurement, or significance testing, is among the most stable of all findings regarding antisocial behavior (Robins, 1991; Rutter, Caspi, & Moffitt, 2003) and results in approximately 6% of male juveniles becoming chronically violent (Dodge & Pettit, 2003). Furthermore, this sex difference is also seen in violent juvenile crime (Dodge & Pettit, 2003; Hinshaw & Lee, 2003; Pettit & Dodge, 2003; Weist & Cooley-Quille, 2001) and in physical aggression (Archer, 2004; Arsenio, 2004; Earls & Mezzacappa, 2002; Hyde, 2005; Rutter, 2003a), thereby adding further support to its validity and importance.

In summary, it is difficult to exaggerate the importance of a thorough understanding of the sex difference in CD for the discipline of clinical child and adolescent psychology. For example, since such substantial sex differences in physical aggression occur as early as ages 2–3 (Archer, 2004; Dodge et al., 2006) and in conduct problems at age 4 (Keenan & Shaw, 2003), Lahey and Waldman (2003) declaimed: “Because the magnitude of these sex differences is considerable, any successful explanation of sex differences will greatly inform general models of the origins of conduct problems.” (p.99). Unfortunately, though Moffitt (2006) has attributed the sex difference to the fact that males are more likely to have the neurodevelopmental risk factors that interact with family adversity, the contribution of biological influences to the differential risk in neurodevelopmental factors has been relatively neglected when compared to the attention accorded to psychosocial factors (Pettit & Dodge, 2003). The importance of addressing such neglect has been underscored by Rutter (2003a), when he speculated that CD might best be viewed as a neurodevelopmental disorder which shares a common etiology with other male preponderant disorders such as autistic spectrum disorders, attention deficit disorders with hyperactivity, and dyslexia. Hence, the goal of the present review is to remedy this neglect by focusing on some “good leads” (Rutter et al., 2003, p. 1092) for the biological influences that contribute to the sex difference in CD.

The Rutter et al. (2003) three level model for conceptualizing the mode of operation of the possible biological influences of the sex difference in CD will provide the basic structural organization for the review because this model, in contrast to other models dealing with biological variables, has been specifically proposed as an attempt to integrate biological variables with the variable of sex differences. In so doing, the review accepts as axiomatic that there is a profoundly complex interplay between biological processes and a myriad of psychosocial and contextual processes (Dodge et al., 2006; Dodge & Pettit, 2003; Granger & Kivlighan, 2003; Hill, 2002; Moffitt, 2005; Raine, 2002b; Rutter, 2003a,b, 2005; Rutter, Moffitt, & Caspi, 2006). It chooses to focus on biological influences because of the relative neglect of this domain, because it is the logical first step for any kind of a comprehensive biopsychosocial model that attempts to integrate all the variables (Hill, 2002; Krol, Morton, & De Bruyn, 2004), and because any adequate treatment of the multiple complex interactions among these processes is beyond the scope of this paper. Also, note that, as with Dodge and Pettit (2003), this review proposes that biological influences result in predispositions that are probabilistically, not ineluctably, related to development of CD. Furthermore, the review will not address the topic of individual differences in developmental pathways to violence because once again, despite the undeniable importance of this topic, it is beyond the scope of the review.

In focusing on biological influences, the review will regard as relevant all of the literature on juvenile antisocial behavior which has been discussed under a wide variety of terms such as: acting-out, aggressive, antisocial, conduct disordered, conduct problems, criminal, externalizing, delinquent, undercontrolled, etc. (Hinshaw & Lee, 2003; McMahon & Frick, 2005). While these various categories cannot be equated and some attempts to give more taxonomic precision to the various terms have been made (Dodge et al., 2006; Hinshaw & Lee, 2003), there is sufficient
overlap among these constructs (Rhee & Waldman, 2002) to justify following the lead of Lytton (1990), and consider
all this literature as relevant to the extent that it sheds light on the possible biological influences which contribute to the
marked sex difference in CD. Also given the vastness of the aforementioned literature and given that the goal of the
review is to be broadly synthetic, the paper will draw on findings of authoritative critical reviews of various domains as
well as individual studies.

The review will begin with an exposition of the three level biological model and the various mechanisms that are
associated with the different levels. In brief, this model proposes that differences in the sex chromosomes (Level 1) give
rise to genetic sex differences and the biological consequences thereof (Level 2) which in turn result in risk mechanisms
(Level 3) that contribute to the marked preponderance of male CD. After presenting this model, the review will then
examine the two broad categories of level three mechanisms that make the greatest contribution to a greater male
prevalence of CD. The first category is an evolved psychological disposition for males to engage in physical
aggression. This disposition will be conceptualized as manifesting itself in three behaviors that increase the likelihood
that males will engage in physical aggression: (a) rough and tumble play, (b) fearlessness, and (c) response to threat.
The second category is the greater male vulnerability to neuropsychological impairment which again will be shown to
increase the likelihood that males will engage in physically aggressive behavior. Evidence for these mechanisms and
their subcategories will be discussed in accordance with the following criteria proposed by Rutter et al. (2003). First, it
must be shown how the proximal mechanisms link up with the first two levels of the causal model and how they
mediate risk or protection. Second, evidence must demonstrate that sexes do indeed differ on the putative mechanisms.
Third, evidence must demonstrate that the mechanisms do provide risk or protection for developing CD.

1. Three level model

This section provides an overview of an adaptation of the three level model which will serve as the basic structure
for the review of the major biological influences on antisocial and violent behavior that have been identified by Raine
(2002b) as: genetic, neuropsychological, neurochemical, psychophysiological, hormonal, and obstetric. These
influences have been conceptualized by Rutter et al. (2003) as operating at three different levels. At the first level, there
is the distal basis starting point which implicates some aspect of the genetic differences between the sexes which stems
from the biological fact of having either an XY or XX sex chromosome complement. At the second level there are the
biological consequences of being male or female such as the differential vulnerability of the sexes to certain physical
hazards. At the third level there are the consequent proximal risk or protective effects of the two levels that are more
directly implicated in the mechanisms which predispose to sex differences in psychopathology such as the greater male
vulnerability to neuropsychological impairment.

In summary then, the review will first discuss the differences in the sex chromosomes (Level 1) which give rise to
genetic sex differences and the biological consequences thereof (Level 2) which in turn result in risk mechanisms
(Level 3) that contribute to the marked preponderance of male CD.

2. Level 1 sex chromosomes

The sex chromosomes are the ultimate biological origin of all sex differences (Arnold, 2004). Approximately
300 million years ago the two human sex chromosomes began to evolve from the same ancestral autosome (Stix, 2004;
Willard, 2003) and thus began a genetic divergence whose results have now been fully decoded (Page et al., 2003,
2005; Ross et al., 2005; Rozen et al., 2003). It is thought that the divergence was initiated by a rearrangement of the Y
chromosome which erected a barrier to recombination between the proto-X and Y chromosomes that initially
encompassed only the sex determining locus on the Y (Ross et al., 2005). Thereafter, subsequence successive
rearrangements on the Y have resulted in markedly reduced meiotic recombination to very small regions of identical
X–Y homology (Jegalian & Lahn, 2001; Skuse, 2005; Willard, 2003). Thus with the exception of the approximately 12
genes in this region and 2 other genes outside this region, most of the genes on the X and Y chromosomes are non-
homologous (Skuse, 2005).

As a result of this dramatically reduced recombination, the Y has little ability to trade defective Y genes for good X
genes with the consequence that it has lost most of the 1000 or so genes it initially had and is currently thought to only
have about 78 genes, most of which are unique to the Y (Skaletsky et al., 2003; Willard, 2003). The enormity of this
evolutionary decline has led to predictions of the eventual demise of the Y. However, this prediction is contradicted by
evidence of a self-repair mechanism for some genes situated within Y-linked palindromic sequences as well as by the fact that of those genes not located in palindromes, not a single one has been lost in 6 million years (Page et al., 2003, 2005; Rozen et al., 2003).

The significance of these findings was lucidly articulated by the team of scientists who cracked the Y’s code. This common substitution of the Y chromosome for the second X dwarfs all other DNA polymorphisms in the human genome. Translating this knowledge into an understanding of the myriad differences between the sexes in anatomy, physiology, cognition, behavior and disease susceptibility presents a monumental challenge, but surely one of broad significance and interest (Page et al., 2003, p. 836).

For the X chromosome, results of the 300 million year divergence have left it with 1098 genes making it among the least gene dense of all the chromosomes, except for the Y, that have been studied to date (Ross et al., 2005). Furthermore, this divergence has resulted in a consequence that rivals the diminution of the Y. The X is the only chromosome which has one of the pair largely inactivated in one sex (female) (Carrel & Willard, 2005; Ross et al., 2005). Such inactivation developed so that both sexes would for the most part have the same dosage of gene products. Inactivation begins early in the development of the female fetus when cells are randomly chosen to inactivate either the maternal or paternal X and the chosen chromosome remains inactive in all subsequent cell divisions (Ross et al., 2005). This results in female genetic mosaicism since inactivation creates a mixture of cells in females which express either their mother’s or father’s X-linked genes (Migeon, 2006). However, recent findings have revealed that X-inactivation is not always complete such that as many as least 25% of the genes on the inactive X are either fully or partially active, with the percentage varying from one woman to another (Carrel & Willard, 2005). Consequently, there is ample scope for the double dose of genes carried on the two female X chromosomes to contribute to differences between the sexes (Federman, 2006).

3. Level 2 genetic sex differences and their biological consequences

The aforementioned sex chromosomal differences result in several genetic sex differences and concomitant biological consequences for males relevant for the paper.

3.1. Male specific SRY gene hormonal consequences

Historically at least, the single most important consequence of having a Y chromosome for males is the influence of the SRY gene. Though a number of genes contribute to sex determination and differentiation (MacLaughlin & Donahoe, 2004; Migeon & Wisniewski, 1998), the SRY gene (SRY stands for sex region on the Y) which is located on the short arm of the Y is the primary sex determinant as it induces the differentiation process of a neutral gonad into testes at 6 weeks (Institute of Medicine, 2001). The lack of the SRY gene results in the gonads beginning the process of becoming ovaries at 12 weeks (Institute of Medicine, 2001). The gonads then become the primary source for prenatal and postnatal hormonal sex differences.

3.1.1. Prenatal and postnatal hormonal differences

Hormones produced by the gonads include androgens such as testosterone, estrogens, such as estradiol, and progestins such as progesterone (Collear & Hines, 1995). All three types of hormones are found in both sexes, though there are differences in the quantity of each hormone present and in the number of receptors for them (Baron-Cohen, Lutchmaya, & Knickmeyer, 2004). Gonadal hormones have two major effects on behavior: prenatal organizational effects which cause permanent changes in brain neural systems and postnatal/pubertal activational effects which are transient and activate existing neural systems (Baron-Cohen et al., 2004; Collear & Hines, 1995; Geary, 1998; Hines, 2004; Maccoby, 1998).

Although male and female fetuses are exposed to androgens, estrogens, and progestins from their gonads as well as from their adrenal glands, placenta, and maternal system, there is a huge difference in the amount of testosterone to which the sexes are typically exposed. At about week 6 of gestation, the SRY gene on the Y chromosome causes the primordial gonads (which are initially the same for both sexes) to differentiate as testes. Shortly thereafter, the male testes begin to pour out abundant amounts of testosterone, with such output peaking at about week 16. This dramatic
hormonal sex difference declines at about week 24 to a much smaller level. It is followed by second postnatal testosterone surge, whose function is not well understood, that continues until about 6 months postnatally (Baron-Cohen et al., 2004; Hines, 2004). Henceforth, these hormonal cascades diminish to low circulating levels of testosterone for both sexes until approximately the start of puberty (Maccoby, 1998). In stark contrast to the testosterone surges which punctuate the development of the male fetus and which are propelled by the testes, the ovaries of the female fetus produce little or no hormones prenatally (Hines et al., 2002). The placenta however does bath both sexes equally in estrogen (Hines, 2004; Institute of Medicine, 2001). At puberty, the hormonal equality of the sexes changes markedly and results in males having at least 20 times more circulating testosterone than females and females converting 200 times more androgen to estradiol than men (Federman, 2006).

It should also be noted that in addition to the direct effects of these gonadal hormones, they can also indirectly contribute to a sex difference by changing the functional role of other hormones. For example, there is evidence that testosterone suppresses and estrogen enhances the hypothalamic–pituitary–adrenal axis thereby possibly rendering females more responsive to the long-term consequences of stress (Rhodes & Rubin, 1999). Similarly, Taylor et al. (2000, 2002) have proposed that whereas estrogen heightens the tend-and-befriend stress response in females, testosterone dampens it in males and thereby increases the likelihood that males will engage in the classic fight or flight response.

3.1.2. Greater male developmental immaturity

Another possible hormonal consequence of having the SRY gene relates to biological maturation. It has long been known that biological maturation in males is much slower than in females (Rutter et al., 2003). Indeed this difference first manifests itself at 4 months prenatally and results in a 4 to 6 week female advantage at birth which increases to a 1 year superiority at age 5 and culminates in a 2 year earlier onset of puberty (Geary, 1998; Tanner, 1978). The biological mechanism that causes this difference is not well understood, though prenatal testosterone may be a factor (Hines, 2004).

3.2. Direct non-hormonal genetic effects on the brain

For a long time it was thought that the foregoing classic view, in which the sex chromosomes operate exclusively through gonadal hormones, explained all biological sex differences. However, recent animal and human studies have found that some cellular sex differences, particularly those in the brain, are induced directly by genes as a result of the different sex chromosome constitution (Craig, Harper, & Loat, 2004; De Vries et al., 2002; McEwen & Lasley, 2005; Vawter et al., 2004). For example, studies of mice (Dewing, Shi, Horvath, & Vilain, 2003) have found 54 genes that work differently in male and female brains just 10 days after conception before any gonadal hormone influence. Moreover, there is also evidence that some X-linked genes are expressed differently, depending on whether or not they are in male or female brains (Skuse, 2005).

Lastly, though it is self-evident that more genes on the X and Y chromosome, such as the Y-linked SRY gene, are involved in the development of sex differences than are genes on the autosomes (Hurst, 2001; Skuse, 2005), it comes as a surprise that there are X-linked, sex specific genes that are expressed exclusively in males as is the case of the many X-linked genes involved in spermatogenesis in mice (Skuse, 2005). This extraordinary situation can occur in a scenario where the same gene can be good for one sex but bad for the other (Hurst, 2001; Skuse, 2005). Take an initially rare recessive gene X-linked gene which would make individuals brightly colored thereby benefiting males by making them more conspicuous and attractive to females but disadvantaging females by increasing the chance of detection by a predator (Hurst, 2001). This gene would be very likely to increase in frequency because in the XY male condition the benefits the gene confers would be expressed, whereas in XX female condition the detrimental effects would be masked by its rarity. However, as the frequency of the gene increases, so will the proportion of females who are homozygous for the gene and hence disadvantaged. Accordingly, natural selection would then promote elimination of the gene in females. Though intriguing, the extent to which this mechanism results in human sex differences is yet to be determined.

3.3. Sex-specific meiotic effects

There are two sex differences in the meiotic mechanisms which produce the gametes (sperm and egg) that contribute to sex differences (Institute of Medicine, 2001). Of those most relevant to this review, the first difference relates to the
number of stem cell divisions that occur to produce the sperm and egg. The average male produces billions of germ cells (sperms) which derive from a population of stem cells that continue to divide throughout the entire life of the male. However, the average female produces only some 500 germ cells (ova) that are arrested at the meiotic prophase of development until ovulation (Institute of Medicine, 2001). Consequently, the much greater number of stem cell divisions in males increases the risk of a copying error which in turn results in a genetic mutation rate that is 5 times higher for males than females (Makova & Li, 2002). Hence the higher mutation rate in males (Crow, 2000) contributes to a greater male vulnerability to various genetic disorders (Rutter, Caspi, & Moffitt, 2003).

Second, there is less recombination over the autosomes during male meiosis than during female meiosis (Institute of Medicine, 2001). Consequently, since recombination is an important genetic repair mechanism and since males are less efficient in this regard, this would appear to be another factor contributing to a greater male vulnerability to various genetic disorders.

Parenthetically it should be observed that this greater male mutation rate has been explained in evolutionary terms as males being the driving force in evolution (Makova & Li, 2002). Thus it is appears that evolutionary processes, beginning with the primal mutation(s) that initiated the divergence of the Y from the X, have selected the male of the species to be the more mutagenic and therefore the more variable, for better or for worse (Archer & Mehdihkhani, 2003).

3.4. Male vulnerability to X-chromosome hemizygotic effects

As previously discussed, the common substitution of the Y chromosome for the second X, which dwarfs all other DNA polymorphisms in the human genome, results in various hemizygotic effects for human males. Namely, since most of the genes on the Y have no copy on the X, the products of these X-linked genes are determined by only half (hemi) of the chromosome complement. However, because females have two X chromosomes, the products of a gene at a particular locus are potentially a function of the respective gene counterparts on both X chromosomes. Thus, females potentially can receive twice the dose of gene products found on the second X (Craig et al., 2004). Because this can be disruptive to the other genes shared by males and females, females have developed processes by which the genes on one of the X chromosomes are inactivated in all somatic cells, though the extent of inactivation is far less than previously thought (Carrel & Willard, 2005).

This mechanism results in two important sex differences. First, it may help explain why more extreme versions of a phenotype may be expressed in males than females (Institute of Medicine, 2001). Since males are hemizygous for X-linked genes that have no Y homologue, they express whatever phenotypes are coded for on the X. Females, in contrast, have two copies of each gene, and hence the effects of the two are averaged (Craig et al., 2004). Therefore, because males express the full, unblunted effect of the single heterozygous allele, they will as a group be more variable and hence more likely to express a more extreme phenotype than females (Rutter et al., 2003; Skuse, 2005).

Second, it helps explain the greater biological vulnerability of males who are 20% more likely than females to die in utero, during infancy and preschool (Migeon, 2006) and who are more vulnerable to most physical hazards such as pregnancy complications, infections, malnutrition, etc. (Rutter et al., 2003). Namely, since males have only 1 copy of X-linked genes, any defective gene mutation always results in the failure of the function encoded by the gene (Migeon, 2006). However, in female carriers of an X-linked mutation, random inactivation of one of the two X chromosomes results in approximately 50% of their cells having the normal gene on the active X chromosome with the mutant gene being on the inactivated X chromosome. Hence, females typically have enough normal cells to perform the function that has been compromised by a defective gene (Migeon, 2006; Puck, 1998). This explains why males usually have a more severe form of X-linked recessive disorders such as hemophilia, Lesch–Nyan syndrome and fragile X syndrome (Migeon, 2006). Moreover, as Migeon (2006) observed, “It does not seem far-fetched to think that cellular mosaicism may have a role in some...sex differences in behavior” (p 1433). The possibility of such a role receives support in the phenomenon of genetic imprinting.

3.5. X chromosome: Genetic imprinting

Genetic imprinting refers to the selective silencing of a gene with respect to expression in the phenotype depending upon whether or not the gene was transmitted by the mother or father, i.e., depending upon whether on not the gene
carries the *imprint* of the mother or father (Arnold, 2004; Pagel, 1999; Plomin, Defries, McClearn, & McGuffin, 2001). Imprinting, if it occurs on the autosomes, would not result in a sex difference, since they are equally transmitted to both sexes (Institute of Medicine, 2001). However, if such imprinting occurs on the X chromosome, it could result in sexually dimorphic expression (Skuse, 2005). For example, if expression of the gene on the maternal X chromosome was imprinted (silenced), this would result in a sexually dimorphic expression since the gene would be silenced in males (who only inherit the maternal X) but not in females who would inherit the gene in a non-silenced form from the paternal X.

### 3.6. X chromosome: Large X effect

A third possible consequence of males having a single X chromosome which in turn might help explain the greater male biological vulnerability is termed the *large X effect*. Namely, genes on the X chromosome, for reasons that are not fully understood, are unusually responsible for viability as well as sterility and incompatibility between the species (Patterson, Richter, Gnere, Lander, & Reich, 2006). This *large X effect* might help explain the greater male biological vulnerability since males, having only one X, might be expected to have diminished viability compared to females.

### 4. Level 3 risk and protective mechanisms

Examination of the consequences of the prior distal levels which result in biologically based proximal risk or protective mechanisms that are more directly implicated in the sex difference in CD constitutes the heart of this paper and will thus be accorded the lion’s share of ink. In order to establish influence at this level, Rutter et al. (2003) established four criteria. First, it must be shown how the proximal mechanisms link up with the first two levels of the causal model and how they mediate risk or protection. Second, evidence must demonstrate that sexes do indeed differ on the putative mechanisms. Third, evidence must demonstrate that the mechanisms do provide risk or protection for developing CD. Fourth, evidence must demonstrate that when the effects of the mechanisms are included in a causal model, they reduce or eliminate the sex difference in CD. This paper will examine and evaluate the evidence for these criteria while bearing in mind the observation of Rutter et al. (2003) that, especially for the fourth criteria, “It is all too clear that few variables have been adequately tested in relation to these rather basic minimal requirements, although research findings do provide some useful leads” (p. 1102).

Hence what follows is a discussion of the proximal risk mechanisms which at the very least provide some *useful leads* in helping to explain the marked male preponderance in CD. The two most important risk mechanisms are (a) an evolved psychological disposition to engage in physical aggression, (b) neuropsychological impairment.

### 5. Evolved psychological disposition to engage in physical aggression

Human aggression can be defined as any behavior directed toward another individual that is carried out with the immediate intent to cause harm (Anderson & Bushman, 2002; Dodge et al., 2006). The type of aggression most relevant to understanding the sex difference in CD is direct, physical aggression which occurs in real world settings. Hence for the purposes of this review, aggression will refer to direct, physical real world aggression. This type of aggression is more common in males at all ages (beginning at ages 2–3), in all cultures, and is most evident in male on male aggression (Archer, 2004; Dodge et al., 2006) with effect sizes generally ranging from moderate (teacher report) to large (peer) for children (Archer, 2004; Hyde, 2005). This large average difference is further magnified by greater male variability thereby making it even more likely that individuals showing high levels of physical aggression will be male (Archer, 2006; Archer & Mehdikhani, 2003). Indeed, aggression in its most extreme forms of same sex homicide and war (Anderson & Bushman, 2002), is virtually an exclusive male phenomenon (Archer, 2004; Buss, 2004; LeBlanc, 2003). In all of the recorded history of the more than ten million animal species, including four thousand mammals which populate the planet, only two species have been documented to engage in warfare, i.e., self-initiated intense territorial aggression of coordinated coalitions resulting in lethal violence to their own species: male chimpanzees and male humans (Buss, 2004; Wrangham & Wilson, 2004).

It will be the contention of this review that evolutionary processes which generated genetic sex differences and resultant biological consequences (Levels 1 and 2) have resulted in the risk mechanism of a greater male disposition to
engage in aggressive behavior. From an evolutionary perspective, aggression can be conceptualized as a solution to adaptive problems, in specific circumstances when the benefits outweigh the costs, such as: co-opting the resources of others, defending against attack, inflicting costs on intrasexual rivals, and negotiating status and power hierarchies (Buss, 2004).

Hence a brief discussion of some of the basic insights yielded by the discipline of evolutionary psychology is in order as many social scientists are unfamiliar with Darwin’s seminal contributions to this discipline as well as the considerable supporting evidence that has subsequently been amassed (Geary, 2004).

5.1. Evolutionary psychology

Evolutionary psychology is the integrative study of behavior and its underlying psychological mechanisms as informed by the insights provided by modern evolutionary theory (Buss & Reeve, 2003). Hence it involves the study of the processes and the products of evolution and the insights these yield with regard to human nature (Buss, 2004). The core predicate of mainstream evolutionary psychological theory is that an adequate explanation of human developmental sex differences requires that the proximate influences on sex-differentiated behavior involving immediate processes such as sex hormones must be related to what are termed ultimate or distal evolutionary processes which have created the proximate processes as each sex has confronted a unique set of adaptive problems during its evolutionary history (Buss, 2004; Wood & Eagly, 2002). One obvious product of these processes is the numerous physical differences between the sexes. However, the evolutionary product which establishes a causal link between the evolutionary processes and sex differences in current behavior is variously termed a psychological mechanism, adaptation, or disposition which is sex-specific (Bjorklund, 2003; Krebs, 2003).

5.1.1. Sex-specific evolved psychological dispositions

A psychological disposition is the fundamental unit of analysis in evolutionary psychology. It refers to a set of procedures within the organism that are designed to process certain information and transform it into behavior that has historically solved adaptive problems in ancestral environments (Buss, 2004; Krebs, 2003). Since humans, like most organisms, have coped with myriad adaptive problems, they have evolved many mechanisms (specific and general) to solve these problems (Buss, 2004; Geary & Huffman, 2002; Nettle, 2006).

Evolved psychological dispositions are conceived of as being significantly different in at least two major ways from the older, now archaic concept of instinct which connotes a behavior that invariably occurs, is context insensitive, and highly rigid. First, some evolved mechanisms are sensitive to specific contexts and hence are activated, or triggered only by certain contexts and after specific information has been transformed through decision rules into an output which can then assume various forms (Buss, 2004). Second, these dispositions can demonstrate phenotypic plasticity (Geary & Huffman, 2002), such that they assume a different manifestation depending upon the environment.

A fundamental principle of evolutionary psychology predicts that the sexes will differ in precisely those domains in which women and men have faced different sorts of adaptive problems, both survival and reproductive. Thus, in evolutionary psychological theory, the likelihood that evolutionary processes would result in identical physical or psychological products in domains in which the sexes have recurrently confronted different adaptive problems and hence employed different adaptive solutions over the long expanse of human evolutionary history is essentially zero (Buss, 1995).

It will be the contention of this paper that such sex-specific dispositions do exist and that they are relevant to explaining the sex difference in CD. The paper will establish this contention in three steps. First, it will establish that the obvious physical sex differences in male size and strength are in part a result of evolutionary selection for bodies disposed for aggression. Second, it will establish that the inevitable corollary of a male body disposed for aggression is a male brain psychologically disposed for aggression. Third, it will then discuss three putative dispositions (rough and tumble play, fearlessness, and response to threat) and provide evidence that links these dispositions to levels 1 and 2.

5.2. Male bodies disposed to aggression

The body dimorphisms most relevant to the sex difference in aggression would include the following. With regard to height, at six feet males outnumber females by a ratio of 2000/1 (Pinker, 2002) and this difference has existed for at
least 3 million years (Arsuage et al., 1997). With regard to strength, the average man is nearly twice as strong as the average woman in chest, shoulder and arm strength (Buss, 2004). With regard other physical differences, in comparison to females, males have 150% greater oxygen capacity, more muscle, larger hearts, and larger lungs relative to body size (Holden, 2004). With regard to the largest sex difference in physical competence, the male superiority in throwing distance and throwing velocity (which manifests itself at age 2) (Hyde, 2005), reaches such an extreme that by age 12 there is almost no overlap between the sexes despite the fact that females have a 2 year edge in physical maturity (Geary, 1998). Hence, it comes as no surprise, that the most common weapon used in male primate and human aggression for eons was *throwing rocks* (LeBlanc, 2003). Because of differences such as these, the athletic achievement gap between the sexes is increasing in all the main running events (except for the marathon where a smaller body frame gives women an advantage on endurance) and has plateaued in all other events, with women performing at about 90% of male levels (Holden, 2004).

One consequence of these dimorphisms as well as the dimorphisms contingent upon reproductive activity has been articulated by Wood and Eagly’s (2002) biosocial model. This model asserts that physical sex differences interact with specific cultural conditions to influence the roles held by men and women because certain activities are more efficiently accomplished by one sex. Participation in these different social roles in turn results in sex differences in psychological dispositions associated with the different social roles. Hence, as predicted by this model, since the physical attributes of physically mature males enable them to more efficiently engage in the activity of physical violence, males have been socialized into such roles and hence in all cultures from for all times have vastly exceeded females in lethal and non-lethal violence.

### 5.2.1. Corollary

An inevitable logical corollary of a male body disposed for aggression has been aptly articulated by Craig et al. (2004) who observed “...it would be remarkable if the obvious anatomical and physiological dichotomy between the sexes arising from evolutionary sexual selection wasn’t paralleled at least to some extent, at the behavioral level” (p. 269).

### 5.3. Male brains disposed to aggression

In contrast to the incontestable existence of body dimorphisms, the existence of evolved, psychological adaptations, mechanisms, or dispositions (Buss & Reeve, 2003; Krebs, 2003) that are sex-specific and hence contribute to the sex difference in physical aggression is far more controversial (Eagly & Wood, 1999; Wood & Eagly, 2002) and hence it will take more discussion to establish the existence of such dispositions. The three dispositions that will be discussed are (1) rough and tumble play, (2) impulsivity/risk taking/fearlessness, (3) response to threat. Doubtlessly there are other mechanisms but these three have been selected because there is substantial evidence to support some of the Rutter et al. (2003) criteria and hence they qualify as useful leads.

#### 5.3.1. Rough and tumble play

Rough and tumble play refers to play that is physical, rough and is exemplified by preschool and juvenile behaviors such as:

- playing ‘ramming’ games of deliberately running into one another, play wrestling, mock fighting, putting clay in one another’s hair, chasing one another around while making machine gun sounds, shooting one another and falling dead, pushing back and forth, convulsing with laughter in the bliss of pretending to make toy horses sneeze and fall down (Maccoby, 1998, p 34).

Though such play is to be distinguished from physical aggression since its intent is not harm but rather a high level of exercise which maximizes the behavioral and morphological characteristics that are useful in competition with other males (Archer, 2004), it should be noted that it frequently puts males “on the verge of aggression” (Maccoby, 1998 p. 51). Furthermore, one of the clearest sex differences in preschool children is that, beginning in the third year, the sexes spontaneously segregate into same sex peer groups with the male peer group predominating in rough and tumble play that occurs much more frequently and vigorously than in the play of females as it also does in the play of nonhuman primates (Geary, 1998; Maccoby, 1998). This segregation and rough-and-tumble play is spontaneous, self-initiating and not primarily a function of differential socialization (Maccoby, 1998, 2000, 2002).
The fact that this sex difference as well as the sex difference in physical aggression is large, emerges almost as soon as children initiate social interactions (age 2), does not seem to be related to differential parental socialization, does not progressively widen as the sexes are exposed to different socialization influences, and has clear cut parallels in chimpanzees, argues strongly for distal evolutionary influences as opposed to exclusive social role influences (Archer, 2004; Maccoby, 1998, 2000, 2002; Pellegrini & Archer, 2005; Wrangham & Wilson, 2004).

Through these rough-and-tumble play episodes boys compete to work out dominance relations (Boulton, 1994) and it is in this context that the sex difference in aggressive behavior is socialized and develops (Pellegrini & Archer, 2005). Thus, it is clear that boys’ rough and tumble play more frequently puts them on the edge of aggression, in a state of greater likelihood that provocations to fighting will occur, than is the case for girls (Maccoby, 1998). From the perspective of evolutionary psychology, the functions of rough-and-tumble large group play include the practice and perfection of complex and fast-paced species-typical motor skills useful in predator avoidance and species specific fighting as well as preparation for the formation of adult coalitions which engage in group hunting and group warfare (Maccoby, 2000; Symons, 1979). Moreover, the finding that from about age 5 onwards boys more often cluster together in larger groups than girls increases the likelihood that they will engage in more organized, coordinated activities as well as the likelihood that they will engage in conflict and competition (Maccoby, 2002). Together these twin tendencies result in males being more likely to engage in dominance aggression which allows the individual to gain the prerogatives that accompany attaining high rank in certain species (Weisfeld, 1994; Wrangham & Wilson, 2004).

In summary, along with Wrangham and Wilson (2004), this review concludes that evolutionary processes have resulted in a biological predisposition for males to engage in dominance aggression which is different in intensity and nature from inter-female status competition in which aggression tends to be more covert and indirect (Pellegrini & Archer, 2005). There is substantial evidence to support two of the Rutter et al. (2003) criteria, namely, that the sexes do differ on a disposition to engage in dominance aggression and this difference clearly increases the risk for engaging in physically aggressive behavior.

Evidence will now be considered that satisfies the third Rutter et al. (2003) criteria of linkage to prior biological levels.

5.3.2. Role of fetal testosterone in brain organization

The role of fetal testosterone in brain organization is the crucial evidentiary domain for addressing the issue of sex-specific psychological dispositions that might be relevant to aggression as it can provide evidence for the “...direct hard-wired coding of sex differences in psychological dispositions and behavior patterns” (Wood & Eagly, 2002 p. 720). Fortunately, there are several current, comprehensive, critical reviews of the extensive animal and human literature on this topic (Baron-Cohen et al., 2004; Berenbaum, 2002; Cohen-Bendahan, van de Beek, & Berenbaum, 2005; Collear & Hines, 1995; Geary, 1998; Hines, 2004; Maccoby, 1998; Ruble, Martin, & Berenbaum, 2006). Hence, this paper does not need to conduct yet another independent review but can draw upon the consensual conclusions of these reviews linking fetal testosterone to rough and tumble play.

Experimental research with animals. Fetal testosterone influences have been studied primarily in rodents (mice, rats, hamsters) and rhesus monkeys. The aforementioned reviews of this literature have unanimously concluded that fetal testosterone has profound organizational influences on behaviors that show sex differences. In particular, treatments of females with testosterone during critical periods of prenatal development produces animals that resemble males in rough and tumble play and in tendencies towards aggression. The experimental nature of the studies makes it possible to rule out psychosocial environmental confounds (a source of contention in human studies) such as differential maternal treatment of infants who are genitally male. For example, in research with rhesus monkeys, the timing of the pharmacological manipulations involving the injection of testosterone into pregnant monkeys can be so calibrated that it produces female infants with a masculinized brain organization whose genitalia are completely female (Maccoby, 1998). Hence the masculinized behaviors of rough and tumble play and aggression which these females exhibit cannot be attributed to any kind of differential maternal treatment elicited by the nature of the genitals.

Correlational research with humans. Most of the evidence from human studies comes from those in females who were exposed to relatively high prenatal levels of testosterone because of congenital adrenal hyperplasia (CAH) (Cohen-Bendahan et al., 2005). CAH is a genetic recessive disorder which involves an inability to produce the adrenal hormone cortisol resulting in female fetuses being exposed to androgen levels similar to those of normal males. This disorder causes genital virilization prenatally and ambiguous genitalia at birth (Hines, 2004). Following birth, the disorder is
typically rapidly diagnosed and the girl is surgically feminized during infancy, reared as a female, and provided with ongoing medical treatment to prevent further virilization. The aforementioned reviews of correlational research with these human subjects have unanimously yielded exactly the same results as the experimental research with animals. Namely, females who were exposed to relatively high prenatal levels of testosterone because of CAH, show higher levels of rough-and-tumble play and increased tendencies to physical aggression when compared to contrast groups of female relatives and unrelated girls matched for age and socioeconomic status who were not so exposed.

Further support for the role of prenatal testosterone in masculinizing the brain comes from studies of gonadally intact males reared as females (Meyer-Bahlburg, 2005), especially those with the medical condition of cloacal exstrophy. This extremely rare condition (about 1 per 400,000 live births) occurs in males who are born with gonads, prenatal sex hormones and hormonal receptors that are normal but are born with ambiguous genitalia (Reiner & Gearhart, 2004). Historically, because reconstruction of the phallus has not been possible, many of these males have their testes removed at birth, have feminizing genitoplasty performed, and are raised psychosocially as females. However, despite surgical and psychosocial efforts, these males raised as females typically exhibited male patterns of rough and tumble play and as many as half of them have spontaneously declared they were boys. These data, despite the inevitable ambiguities of a correlational study and with full recognition that gender identity involves more than prenatal androgen, adds further support to the masculinizing role of prenatal testosterone on the male brain (Berenbaum & Sandberg, 2004; Meyer-Bahlburg, 2005).

Convergence of animal and human research provides strong evidence for the hard-wiring of aggressive behaviors and rough and tumble play which increases the risk that males will engage in aggressive behavior especially since the longstanding objection that differential parental treatment might explain the sex difference in rough play and male-typical toy play which increases the risk that males will engage in aggressive behavior especially since the longstanding objection that differential parental treatment might explain the sex difference in rough and tumble play (Quadagno, Briscoe, & Quadagno, 1977) has been effectively rebutted by the following findings (Cohen-Bendahan et al., 2005; Hines, 2004).

First, parents of CAH girls were given medical advice to encourage feminine development in their daughters which they reported they followed. It is of course possible that parents were inaccurate in their reporting or defied medical advice. However, compelling evidence against differential parental socialization comes from two recent observational studies of CAH girls: (a) CAH girls did not play more with boys’ toys when a parent was present than when they played alone (Servin, Nordenstrom, Larson, & Bohlin, 2003). (b) Parents did not encourage more male-typical toy play in their CAH girls as opposed to their unaffected sisters (Pasterski et al., 2005).

Second, there is no correlation between degree of genital virilization and masculinized behavior (Hines, 2004), degree of atypical gender identity (Berenbaum & Bailey, 2004) or level of psychological adjustment (Berenbaum, Korman, Duck, & Resnick, 2004). Therefore, it is unlikely that psychosocial responses to genital virilization account for subsequent masculinized behavior, either through differential parental socialization, masculinized gender identity, or an interaction between the two.

Third, consistent with findings in other species, males with CAH have generally been found to be similar to their unaffected brothers in sex-typed play and aggression (Cohen-Bendahan et al., 2005). This finding, which has typically been interpreted to mean that once a certain threshold of fetal testosterone has been reached for males, levels beyond this have no additional masculinizing effects, makes it unlikely that the findings for CAH girls are due to the illness itself.

Fourth, studies of females who were exposed to relatively high prenatal levels of testosterone also include those whose exposure was due to treatment of their mothers with a form of androgen-based synthetic progestin in the mistaken belief that such treatment would help maintain difficult pregnancies. Females exposed to these androgenic progestins resemble CAH girls in that they are born with virilized genitalia and exhibit elevated tendencies towards physical aggression, higher levels of tomboyism, and preferences for male typical toys and playmates (Collear & Hines, 1995; Hines, 2004). However, in contrast with CAH girls, this kind of exposure does not require ongoing medical treatment to prevent virilization (Reinisch & Karow, 1977). This finding renders less likely the parental differential socialization explanation since the findings were the same as those of studies of females with CAH despite the fact that parental concern regarding the issue of virilization in the studies of females with progestin-induced effects would presumably be far less than that of parents of CAH girls.

In summary, it warrants repeating that the convergence of animal and human research provides convincing evidence for the hard-wiring of a male psychological disposition to engage in aggressive behaviors and rough and tumble play. The third Rutter et al. (2003) criterion seems to have solid scientific support since this disposition is clearly linked to the two prior biological levels through the role of the Y chromosome (level 1) which results in the fetal difference in testosterone (level 2).
5.3.3. Fearlessness

Of all the psychophysiological correlates of antisocial behavior that have received considerable theoretical and empirical attention for several decades, low resting heart rate, which is thought to reflect a more generalized low physiological arousal, is the best replicated (Lorber, 2004; Ortiz & Raine, 2004; Raine, 2002a,b). Moreover, this relationship seems to be causal since it predicts adult antisocial behavior from childhood measures and cannot be explained away as artifactual (Ortiz & Raine, 2004; Raine, 2002a). The most likely explanation for this causal relationship is a fearless temperamental style (McMahon & Frick, 2005; Nigg, 2006a; Raine, 2002a) characterized by a preference for novel, exciting dangerous activities, less reactivity to threatening and emotionally distressing stimuli, and less sensitivity to cues of punishment.

As with rough and tumble play, beginning at age three, a robust sex difference emerges, with males having lower resting heart rates than females (Raine, 2002a). A related sex difference exists in empathy such that beginning in childhood males show less concern than females about the harm their aggression might bring to others (Archer, 2004; Baron-Cohen, 2003; Keenan & Shaw, 2003). Hence, Archer (2004) has proposed that a probable mechanism contributing to the sex difference in aggression is the greater male willingness to take risks as they are less deterred than females by fearfulness and empathy. This disposition for engaging risky behavior is also consistent with findings that impulsiveness and lesser weighting of long term consequences are associated with greater male violence (Archer, 2004).

With regard to a possible linkage to prior biological levels, there is evidence indicating that higher levels of fetal testosterone are associated with poorer quality of social relationships (Baron-Cohen et al., 2004; Knickmeyer, Baron-Cohen, Raggat, & Taylor, 2005). Additional evidence involving genomic imprinting is provided by a study of females with Turner’s syndrome which is characterized by an incomplete or absent second X chromosome (XO) (Skuse, 2005). Skuse et al. (1997) found that the rate of offensive or disruptive behavior (McGuffin & Scourfield, 1997) was greater when the X chromosome was inherited from the mother rather than the father. Thus, in effect, the maternal XO females behaved similarly to males who only inherit the maternal X (Pagel, 1999). This finding suggested existence of a gene(s) on the X chromosome for a set of cognitive skills for social communication which is maternally imprinted. Because of this maternal imprinting, only the gene(s) on the paternal X would be expressed and thus the gene(s) would only be expressed in females who always receive the paternal X and not in males who never receive the paternal X. Such a mechanism would make sense in evolutionary terms if females have been selected to have greater social skills than males (Pagel, 1999). This intriguing possibility is in need of replication (Craig et al., 2004).

In summary, there is a significant level of empirical support for some of the Rutter et al. (2003) criteria which suggests that the sex difference in fearlessness contributes to and is part of the ensemble of rough and tumble behaviors which puts boys “on the verge of aggression” (Maccoby, 1998, p.51).

5.3.4. Response to threat

One of the most consistent findings of laboratory studies of aggression is that perception of threatening provocations leads to retaliatory aggression (Coe & Dodge, 1998). Recent findings have provided support for this mechanism. Research with male rats found that rapid increases in corticosteroids caused by stressors unrelated to fighting precipitated violent behavior by lowering thresholds for attack (Kruk, Meelis, Halasz, & Haller, 2004). Furthermore, the study also found evidence that the brain’s aggression system worked not by controlling motor responses but by changing the rat’s perception such that once a threat is perceived, they will attack (Adelson, 2004). This swift, aggressive response to threat represents an evolutionary adaptation since such situations require fast responses to be effective and also require that the responses continue until the threat is successfully vanquished since stopping halfway is dangerous (Adelson, 2004). Similarly, Boyce and Ellis (2005) have provided impressive empirical support for their contextual theory of the origins and functions of stress reactivity. This theory proposes that in certain contexts biological reactivity to psychological stressors can increase adaptive competence in highly stressful environments by augmenting vigilance to threats and dangers.

With regard to a sex difference in this mechanism, Taylor et al. (2000, 2002) have proposed that whereas males commonly respond to stress with the classic flight or fight response which is “…at least, in part, organized and activated by androgens” (p.417), females commonly respond with a tend and befriend response. Their theory is supported by meta-analyses of laboratory studies of emotional arousal which found a large sex difference in aggression favoring males in contexts in which provocative stressors were either not present or ranged from small or moderate (Bettencourt & Miller, 1996; Knight, Guthrie, Page, & Fabes, 2002). This finding was interpreted as reflecting a male disposition to perceive a situation as more threatening and to be less fearful of retaliation. The antecedents of such a disposition
appear shortly after birth such that males are more quickly and easily aroused by relatively strong stimuli, take longer to return to baseline levels, and are less capable of inhibiting certain types of emotional-related responses than are females (Knight et al., 2002).

With regard to a possible linkage to the prior biological levels, a possible connection has been established between a variation for a X-linked gene that codes for the enzyme monamine oxidase A (MAOA) and aggression (Meyer-Lindenberg et al., 2006; Miczek & Fish, 2005). MAOA is a key enzyme in the catabolism of monamines such as serotonin and provides the major clearing step for serotonin during brain development (Meyer-Lindenberg et al., 2006). Earlier studies linked genetic deficiencies in MAOA activity to increased serotonin levels during brain development with subsequent development of aggression in mice and humans by causing neural hyperactivity to threat (Caspi et al., 2002; Meyer-Lindenberg et al., 2006; Miczek & Fish, 2005; Moffitt, 2005). However, it was the landmark study of Caspi et al. (2002) which provided impressive confirmation of this linkage as it reported the first instance of an interaction between a measured gene and a measured environment in the behavioral sciences (Moffitt, 2005). Caspi et al. (2002) found that males having the low activity variant of MAOA (MAOA-L) and hence higher levels of serotonin during brain development, and who were subjected to stress of maltreatment (e.g., maternal rejection, harsh discipline, physical abuse), were much more likely to have engaged in violent behavior than those who had the high activity variant. Only males were studied since MAOA is an X-linked gene and hence only males with the low polymorphism variant will inevitably have deficient MAOA activity. This finding has been replicated in the majority of subsequent studies (Meyer-Lindenberg et al., 2006), the most important of which for the purposes of this paper is that of Meyer-Lindenberg et al. (2006). Their study of normal adult male and female volunteers found those with MAOA-L had differences in brain structures which predicted greater emotional reactivity and deficient inhibitory cognitive control. Furthermore, and most importantly, they not only concluded that these findings were more pronounced for males with MAOA-L, but that males in general have intrinsically weaker emotional regulatory controls. Since approximately one-third of males carry the low-activity version of the gene (Caspi et al., 2002; Foley et al., 2004) and since males in general may have weaker regulatory controls (Meyer-Lindenberg et al., 2006), males would seem to be more likely to inherit a genotype that is highly reactive to stress and hence more biologically vulnerable than females to developing CD. As Foley et al. (2004, p. 743) noted “...MAO-A is an X-linked gene, and an increased risk for conduct disorder in association with an interaction between MAO-A and exposure to adverse childhood environments suggests that there are sex differences in the heritable transmission of risk to male and female offspring.”

In summary, there is a significant level of empirical support for the Rutter et al. (2003) criteria and thus it would seem reasonable to assume that the sex difference in responding to threat adds to the ensemble of rough and tumble play and fearlessness which puts boys “…on the verge of aggression”(Maccoby, 1998, p. 51).

6. Neuropsychological impairments

Beginning with the seminal work of Moffitt (1993a,b), reviewers have unanimously concluded that some form of neuropsychological impairment is involved in the etiology of CD (Coie & Dodge, 1998; Dodge et al., 2006; Hill, 2002; Hinshaw & Lee, 2003; Ishikawa & Raine, 2003; Moffitt, 2006; Morgan & Lilienfeld, 2000; Raine, 2002a,b; Raine et al., 2005; Rutter, 2003a). The mechanism of neuropsychological impairment is commonly thought to mediate risk for CD by causing deficits in executive and cognitive functioning, with deficits in the verbal domain being the most well established (Dodge et al., 2006; Hinshaw & Lee, 2003; McMahon & Frick, 2005; Nigg & Huang-Pollack, 2003; Rutter, 2003a). Hence, this review will focus on these deficits while recognizing that there may also be deficits in spatial and memory functions (Raine et al., 2005).

Once again, according to the criteria established by Rutter et al. (2003), it must be shown (a) how the mechanisms of neuropsychological impairment mediate risk for CD, (b) that sexes do differ on the putative mechanisms, and (c) how the mechanisms link up with the first two levels of the causal model.

6.1. Executive dysfunction

Though agreement is lacking on the number and nature of processes which constitute executive functioning, there is a consensus that such processes enable the self regulation necessary to successfully achieve future goals (Barkley, 2006a; Biederman et al., 2004; Nigg, 2006b) and that their impairment increases the likelihood of emotional, behavioral, cognitive dysregulation (Hinshaw & Lee, 2003; Rutter, 2003a) with the resultant development of oppositional and defiant
behavior that increases the risk for developing CD (Coie & Dodge, 1998; Hurley & Eme, 2004; Reiff & Tippins, 2004). The most well-known, well documented biological cause of executive function deficits is ADHD (Barkley, 2006c; Brown, 2005; Ishikawa & Raine, 2003; Nigg, 2006b).

6.1.1. ADHD

There is a robust consensus that ADHD is a developmental disorder characterized by deficits in executive functioning (Barkley, 2006c; Brown, 2005; Nigg, 2006b) and that genetic and neurological factors make the greatest contribution to the disorder (Barkley, 2006d; Biederman & Farone, 2005). Furthermore, the principle symptoms of ADHD such as hyperactivity, impulsivity and deregulated, negative emotionality are the most commonly cited risk factors in the development of CD (Barkley, 2006c,d; Frick, 2004; McMahon & Frick, 2005; Nigg, 2006a; Reiff & Tippins, 2004). In addition, there is mountainous evidence that the combined type of ADHD is an exceedingly common co-morbid condition of CD with estimates typically ranging from 20% to 50% (Barkley, 2006b; Lynam, 1996; Waschbusch, 2002) and in some studies approaching 100% (Klein et al., 1997; Lahey, Loebur, Burke, & Applegate, 2005).

What remains in dispute is how to understand the exact nature of this co-morbidity. McMahon and Frick (2005) explain the co-morbidity in terms of ADHD being a developmental precursor to CD. Nigg (2006a) suggests that the co-morbidity can be partially accounted for by the overlap of ADHD and CD on temperamental dimension he terms Approach which takes the form of impulsivity. Barkley (2006b) however contends that the co-morbidity represents a unique disorder in its own right. Regardless of how this dispute may resolve itself, it is beyond cavil that individuals who are co-morbid for ADHD and CD display a more pernicious form of antisocial behavior than those with a single disorder in terms of a greater range, severity and persistence of antisocial activity and greater academic impairment (Barkley, 2006b; Himshaw & Lee, 2003).

There is also a robust consensus that the combined type of ADHD is three times more common in males than females in epidemiological studies in which referral bias is unlikely to account for the preponderance (Barkley, 2006a; Reiff & Tippins, 2004; Rutter et al., 2003), is not eliminated when sex-specific norms are used for identification (Waschbusch & King, 2006), and reaches an astonishing male/female ratio of 16:1 when the ADHD is pervasive (Rutter et al., 2003).

In summary, there is a solid body of evidence that ADHD satisfies the criteria of a definite sex difference on a mechanism that increases the risk for developing CD. Furthermore, there is even some evidence that ADHD satisfies the criterion that when the sex difference in ADHD is statistically controlled for, there is a corresponding reduction in the sex difference in CD (Rutter et al., 2003). However, satisfaction of the criterion of a linkage of ADHD to prior biological levels which would explain the sex difference in prevalence is elusive, though two possibilities suggest themselves.

First, a recent meta-analysis of studies of sex differences in temperament (which was defined as a biologically based emotional and behavioral consistency that appears early in life that can influence the development of psychopathology) has provided a plausible biological explanation for the sex difference in ADHD (Else-Quest, Hyde, Goldsmith, & Van Hulle, 2006). The meta-analysis concluded that there was a large difference disfavoring boys in a temperamental factor designated effortful control which included the dimensions of attention regulation and inhibitory control. Furthermore, this same factor is cited by Nigg (2006a) as a major temperamental contribution to the development of ADHD. As deficits in attention regulation and inhibitory control represent two of the core symptom domains of ADHD (Barkley, 2006a) and as a commonly accepted theory of ADHD is that it represents the extreme end of a continuum (Barkley, 2006a; Nigg, 2006a; Rutter et al., 2006), it would appear that a plausible biological explanation for the sex difference in ADHD is that it reflects the extreme version of the sex difference in the biologically based temperamental dimension of effortful control. However, the biological basis for the sex difference in effortful control is not known.

Second, some research suggests that, in accordance with the polygenetic threshold model of sex differences (Eme, 1992), males have a lower threshold for expression of the disorder in their phenotype (Barkley, 2006d). But again, even if this is the case, the biological basis for this threshold sex difference is not known.

In summary, there is strong empirical support for two of the criteria to establish ADHD as a proximal risk mechanism for CD as the sexes do markedly differ in the prevalence of ADHD and ADHD clearly increases risk for CD. However, linkage of ADHD to a sex difference to prior biological levels is seminal and there is but a single study that provides some evidence for the reduction of the sex difference in CD when ADHD is controlled for. Lastly, it should be noted that although ADHD clearly contributes to the executive function deficit in CD, it cannot adequately explain all such deficits (Raine et al., 2005).
6.1.2. Cerebral insults

Since executive functions are the most sensitive of all cognitive functions to acquired cerebral insult (Stuss & Levine, 2002), it follows that such insults commonly result in deficits in executive functioning. Of the innumerable hazards that can inflict such insults, pride of place is accorded to prenatal and perinatal complications as their link with antisocial behavior has been securely established by several studies (Dodge et al., 2006). These insults may account for as much as 20% of cases of ADHD (Barkley, 2005; Max et al., 2004) and can cause a variety of other problems such as hyperpersistent or disinhibited behavior, deficits in sustained attention, impaired ability to delay gratification, or difficult temperament which in interaction with environmental adversity can increase the risk of CD (Beck & Shaw, 2005; Dodge & Pettit, 2003; Raine, 2002a,b; Rutter, 2003a). Furthermore, since as previously discussed, males are more vulnerable than females to a host of hazards which can cause such insults, acquired cerebral insults satisfies three of the criteria for a mechanism in that there is a sex difference linked to prior biological levels that increases the risk for CD.

6.2. Verbal deficits

A substantial literature has implicated cognitive deficits in the verbal domain as influences in the development of CD (Hill, 2002; Hinshaw & Lee, 2003; Lahey & Waldman, 2003; Nigg & Huang-Pollack, 2003; Rutter, 2003a). Two major mechanisms have been adduced to explain this linkage (Hill, 2002; Nigg & Huang-Pollack, 2003). First, deficits in verbal reasoning may reduce self-control and problem solving abilities and thereby weaken children’s adaptive capability to adverse environments. Second, these deficits may precipitate negative socialization processes, especially those involved in school failure. Therefore, the first criterion of establishing how cognitive deficits might mediate increased risk for CD would seem to be satisfied.

The second criterion of establishing a sex difference in verbal deficits would also seem to be satisfied. First, with regard to reading comprehension, the mean difference favoring females when combined with greater male variance results in three boys for every two girls in the lowest 10% (Geary, 1998). Second with regard deficits such as verbal learning disabilities, stuttering and dyslexia, comprehensive reviews have consistently concluded that throughout the English-speaking world males outnumber females by ratios of at least 2:1 (Halpern, 2000; Liederman, Kantrowitz, & Flannery, 2005; Rutter et al., 2004).

The third criterion of linking this difference to prior biological levels has several possible mechanisms for which there is significant empirical support. First, as previously discussed with regard to deficits in executive functioning, the greater male vulnerability to numerous physical hazards can be expected to similarly increase the male susceptibility to deficits in verbal functioning. Second, the greater likelihood of more extreme versions of a phenotype being expressed in males than females provides an explanation for the substantial difference in extreme scores for males as compared to females not only on verbal ability but also other cognitive and academic tests (Archer & Mehdikhani, 2003; Arnold, 2004; Geary, 1998; Hedges & Nowell, 1995; Nowell & Hedges, 1998). This mechanism is especially relevant for extremes of cognitive abilities since it appears that evolution has favored the development of X-linked genes that are associated with higher cognitive abilities as indicated by the large number of X-linked mental retardation syndromes (Skuse, 2005). Males are more likely than females to show deficits in cognitive abilities caused by deleterious mutations and for the same reason are also more likely to express the genes associated with exceptionally high abilities (Skuse, 2005). Third, there is support for the hypothesis that high levels of male testosterone slows the rate of development of the left hemisphere and thereby increases the risk interval for exposure of the hemisphere to adverse intrauterine events (Baron-Cohen, Knickmeyer, & Belmonte, 2005; Baron-Cohen et al., 2004; Halpern, 2000). This increased risk interval translates into a greater risk of language impairment for males as it is the left hemisphere that primarily mediates most aspects of language functioning (Gazzinga, 1998; Halpern, 2000).

7. Conclusions and future directions

There is a strong scientific consensus that life-course-persistent CD represents the most virulent type of CD that this type of CD is virtually an exclusive male phenomenon, and that biological variables play a major role in its development. This review attempted to provide some useful leads for identifying the precise biological influences which help explain why CD is almost exclusively a male disorder. In so doing, it hopefully contributed to the development of an emerging general consensus model of CD (Dodge et al., 2006).
Excellent directions for discovering additional useful leads for biological influences that contribute to the sex difference in CD as well as for the wide range of psychosocial influences that are implicated in aggressive and antisocial behavior in general have been set forth by Rutter et al. (2003), Moffitt (2006) and Dodge et al. (2006). This review would suggest three addenda to their agendas. First, since the most convincing research linking Level III mechanisms to Level I and II mechanisms involves girls with CAH, future research should be expanded to include the assessment of variables such as responses to stress and fearlessness. Since these variables, along with rough-and-tumble play, are major influences in putting boys on the verge of aggression, their linkage to fetal testosterone levels would solidify their biological basis. Second, future research needs to explore the implications of the recent astounding discovery that females have about 25% more active genes than males. Third, the findings linking CD to \textit{MAOA} warrant additional replications and extension.

Lastly, since one of the ultimate goals of research on sex differences and psychopathology is to provide recommendations for interventions to minimize problems and enhance well-being (Zahn-Waxler, Crick, Shirmeliff, & Woods, 2006), this review will conclude with some implications for treatment. Though treatment is beyond the purview of this review, offering a few implications would seem appropriate in light of the fact that interventions are so rarely examined in relation to gender (Zahn-Waxler et al., 2006).

Moffitt (2006, P. 582) observed that the antisocial personality of those with CD is “...slowly and insidiously constructed, and accumulating consequences of the youngster’s personality problems prune away options for change.” The first recommendation is anchored in the review’s conclusion that the slow, insidious construction of CD is influenced by biologically based psychological dispositions that increase the likelihood males will engage in physical aggression. Though most children exhibit low levels of physical aggression from the earliest time that it can be accurately measured (24 months) through early childhood (3rd grade), a small percentage of children (6%) who are mostly male show a high stable pattern of aggression (NICHD, 2004). It is precisely this small group who become highly troublesome to peers, parents, and teachers (Dodge et al., 2006) and who are most likely to continue to their aggression into late adolescence and early adulthood (Watson, Fischer, Andreas, & Smith, 2004). In short, there is an obvious behavioral marker for the emergence of the “few, persistent and pathological” (Moffitt, 2006, p. 571) who eventually account for more than 50% of crimes in the United States (Moffitt, 2005). Interventions need a laser-like focus on this group.

The second recommendation is that mental health professionals need to fully recognize that those with CD do have neuropsychological impairments, such as verbal deficits and ADHD, which must be addressed. This is especially true with regard to ADHD not only because of its extensive co-morbidity with CD but also because it is eminently treatable (Biederman, Spencer, Wilens, Prince, & Farone, 2006; Smith, Barkley, & Shapiro, 2006a).

In summary, beginning in toddlerhood, highly aggressive males who exhibit significant indications of verbal deficits and ADHD behaviors need to be identified and treated because the slow, insidious antisocial development that yields the few, the persistent, the pathological is well under way. Effective interventions exist (Dodge et al., 2006), but as always, the biggest intervention challenge will be to find effective means for helping families to cooperate with such interventions (Rutter, 2003a). Witness the recent failure of a model preschool intervention for hyperactive/aggressive children in which “...more than 60% of parents did not attend training classes regularly, if at all” (Smith, Barkley, & Shapiro, 2006b, p. 681).

References


