BOOK CHAPTER

Antisocial and Callous Behaviour in Children

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Antisocial and Callous Behaviour in Children

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ABSTRACT

Antisocial behaviour is one of the most common reasons for a childhood referral to mental health and educational services and represents a substantial public health cost. Callous-unemotional traits can be used to distinguish between children who are capable of pre-meditated antisocial behaviour and violence and children whose antisocial behaviour and violence are primarily impulsive and threat reactive. Decades of developmental psychopathology research have shown that children with antisocial behaviour are thus a heterogeneous group and, for interventions to be successful, it is critical that distinct subgroups of children receive services that best match their profile of vulnerabilities and strengths. Recent advances in genetic and brain imaging research in the field have made important contributions to our understanding of the developmental vulnerability that callous-unemotional traits represent. In this chapter, we provide an overview of the current evidence base with regard to genetic and neuroscience findings of callous-unemotional traits and antisocial behaviour with callous-unemotional traits. We also discuss the implications of these findings for prevention and intervention, and finish by outlining what we consider to be necessary directions for future research.

KEYWORDS: Antisocial behaviour; callous-unemotional traits; genetic research; magnetic resonance imaging research

Introduction

Antisocial behaviour is one of the most common reasons for a childhood referral to mental health and educational services and represents a substantial public health cost (Scott et al. 2001). We know that children with early-onset antisocial behaviour are at risk of developing chronic life-course persistent antisocial problems, as well as several other psychiatric and physical health problems (Kim-Cohen et al. 2003; Odgers et al. 2007). It is also evident from decades of developmental psychopathology research that children with antisocial behaviour are a heterogeneous group and, for interventions to be successful, it is critical that distinct subgroups of children receive services that best match their profile of vulnerabilities and strengths (Frick and Viding 2009).

Callous-unemotional (CU) traits (lack of guilt and empathy, as well as shallow affect) can be used to distinguish between children who are capable of pre-meditated antisocial behaviour and violence (high CU-subtype; AB-HCU) and children whose antisocial behaviour and violence are primarily impulsive and threat reactive (low CU-subtype; AB-LCU). Adults with a combination of CU traits and antisocial behaviour are labelled psychopaths within the criminal justice system. The first extension of the psychopathy concept to children was Bowlby's (1946) description of 'affectionless psychopathy'. It mirrored some of the key features introduced in 1941 by Cleckley in his seminal work *The Mask of Sanity* (such as lack of responsiveness to suffering of others), but lay forgotten for a long time until the extension of psychopathy construct to children was proposed again by Frick and colleagues (1994). While it would be entirely inappropriate to suggest that children are psychopaths, it is the case that there is a subset of children with severe conduct problems[1] *and* CU traits that place them at heightened risk for developing adult psychopathy (Lynam et al. 2007). CU traits are currently being considered as a subtyping criterion for the fifth edition of the Diagnostic and Statistical Manual-V of the American Psychiatric Association (Frick and Moffitt 2010; Sherer and Nickerson 2010).

[1] Please note that the terms antisocial behaviour and conduct problems will be used interchangeably in this review

Longitudinal data show that children with AB-HCU present with a more severe behavioural profile and more long-term problems than children with AB-LCU (Fontaine et al. 2011; Frick and Viding 2009). Even in the absence of AB, CU traits are associated with poorer outcomes, including risk for developing delinquent behaviours and other types of psychosocial maladjustment (e.g. Barker et al. 2011; Frick et al. 2003; Kumsta et al. 2012; Rowe et al. 2010). Longitudinal data also show that CU traits add to the prediction of serious and persistent criminal behaviour in boys (Pardini and Fite 2010). Furthermore, CU traits have been shown to be associated with overt aggression, delinquency and behavioural dysregulation (Lau and Marsee 2012). In short, the affective characteristics of psychopathy (CU traits) can be delineated in children and may be a risk index for later psychopathy, as well as other forms of poor outcome.

Cognitive experimental data suggest that children with AB-HCU are poor at modulating their behaviour in response to punishment in conditioning paradigms (Frick and Viding 2009). In addition, they have difficulties in recognising others' fearful and sad facial expressions and vocal tones (Blair and Viding 2008), show impaired/reduced affective empathy responses to other people distress (De Wied et al. 2012; Schwenck et al. 2012) and report lower levels of empathic concern and sadness in response to other's distress (Pardini and Byrd 2012). In contrast, AB-LCU is associated with an exaggerated affective response to perceived social threat, such as anger or in some cases even ambiguous, neutral expressions (Dadds et al. 2006; Frick and Viding 2009).

Recent findings suggest that children with AB-HCU may also have an impoverished personal experience of fear and guilt, which could in part explain why they have such difficulty perceiving others' distress (Jones et al. 2010; Marsh et al. 2011b). Children with AB-LCU report comparable experiences of fear and guilt to typically developing children. Interestingly, Jones et al (2010) found that neither group of children with antisocial behaviour has difficulties in 'mentalising' (perceiving the thoughts and intentions of other people). It is possible therefore that the difficulties that children with AB-HCU exhibit are limited to 'feeling what others feel' and do not extend to difficulties commonly seen in children with autism spectrum disorders, i.e. 'knowing what others think'. This pattern of difficulties and strengths may explain why children with AB-HCU are good at manipulating others to their own advantage, even if such behaviour

will cause distress to somebody else. Theoretical accounts of AB-HCU propose that normal socialisation is disrupted in these children because they do not form adequate associations between their transgressions and punishment outcome / other people's distress (a form of social 'punishment') (Blair and Viding 2008). By contrast, children with AB-LCU are proposed to form 'hostile attribution biases' and to exhibit aggression as a result of living in unstable and threatening environments (Blair and Viding 2008; Dodge and Crick 1990; Frick and Viding 2009). It also seems to be possible that AB-HCU and AB-LCU children show distinct expectations regarding the consequences of their aggressive behaviour. Recent research has shown that children with AB-HCU are less likely to expect that aggression results in victim suffering, are less concerned about it or about punishment or feelings of remorse, and are more likely to expect that it results in peer dominance. In contrast, children with AB-LCU were more likely to expect that attacking aggressive behaviour towards other people would reduce their aversive behaviour (Pardini and Byrd 2012).

Aetiology of CU traits

A number of twin studies have examined the aetiology of CU traits in children and youth. These studies come from the United States, Sweden and United Kingdom. The samples used in these studies vary in size from moderate (398 twin pairs) to large (3687 twin pairs), represent different age ranges (7-24 years old) and have used a range of instruments that have relied on both self and other (parent or teacher) ratings. In this chapter we will concentrate specifically on genetically informative data on CU traits or AB-HCU, as CU traits represent the core affective features of psychopathy (Frick & Viding, 2009).

Twin studies estimate heritability by comparing the degree to which identical twins (who effectively share 100% of their polymorphic genes) as compared with non-identical twins (who on average share 50% of their polymorphic genes) are similar to each other. If identical twin similarity exceeds non-identical twin similarity, then heritable influences on a trait are inferred. The existing studies have reported remarkably consistent results of moderate to strong heritability for CU traits in children and youth. These studies estimate that 40-78% of variation in CU traits across the population is due to genetic influences (Bezdjian et al. 2011; Blonigen et

al. 2005, 2006; Fontaine et al. 2010; Larsson et al. 2006; Taylor et al. 2003; Viding et al. 2007). Our own data from the Twins Early Development Study (TEDS) has also indicated that at age seven the group difference between those scoring at the high end for CU traits (top 10%) and other children is also largely driven by genetic influences (h_g^2 = .67; Viding et al. 2005). These group heritability estimates appear very similar regardless of whether the CU occurs with (h_g^2 = .80) or without (h_g^2 = .68) elevated levels of conduct problems (Larsson et al. 2008).

Twin studies are also important for documenting the extent to which environmental factors influence individual differences or group differences in CU traits. Shared environment in twin studies refers to environmental factors that make the members of the twin pair more similar than would be expected by genetic relatedness alone (crudely, this can be inferred if non-identical twin similarity exceeds 50% of identical twin similarity, as would be expected if only genetic influences were driving twin similarity). Non-shared environment in twin studies refers to environmental factors that make members of the twin pair dissimilar to each other (crudely, this can be inferred if identical twin similarity is less than 100%). Modest shared environmental influences were detected in only few cases for CU (Fontaine et al. 2010; Viding et al. 2007), but our longitudinal data (described more fully below) indicate that such influences may be particularly important for a handful of girls who have stable and high levels of CU. All studies, including our own, have demonstrated that non-shared environmental influences are particularly important for the development of CU. This does not mean that family or neighbourhood environments are not relevant for development of CU. Rather it suggests that environmental risk factors, including those experienced within the family context, are likely to promote differences between members of the same family (non-shared environment in the twin models). The magnitude of the heritability and environmental estimates for CU traits from child and adolescent samples are in line with previous adult twin data on psychopathic personality traits (Blonigen et al. 2003), as well as other personality dimensions (Bouchard Jr and Loehlin 2001).

Are there sex differences in the aetiology of CU traits?

Four studies to date (Bezdjian et al. 2011; Fontaine et al. 2010; Larsson et al. 2007; Viding et al. 2010) have incorporated dizygotic opposite-sex twin pairs in their analyses and formally explored the potential role of qualitative sex differences (i.e., different genes and environments

influencing phenotypic variation for males and females). None of these studies reported qualitative sex differences for CU traits. A number of studies have also assessed the possibility of quantitative sex differences (i.e., the same genetic and environmental influences affecting males and females to a different degree). Two studies found little evidence of quantitative sex differences for CU traits (Blonigen et al. 2006; Larsson et al. 2006), but there is also some support for a higher heritability of CU for males (Bezdjian et al. 2011; Fontaine et al. 2010; Viding et al. 2007). For instance, using data from 9462 youths from the Twins Early Development Study (TEDS), Fontaine et al. (2010) found that strong heritability (h^2 = .78) was observed for boys on a stable high CU trajectory (between 7 and 12 years old). Stable and high levels of CU in girls, however, appeared to be almost entirely driven by shared environmental influences (c^2 = .75). Replication of this finding is needed given the small number of children who followed the stable and high CU trajectory, and even smaller proportion of this already small group who were females (less than 1% of the total sample).

Stability of CU traits: Genetic and environmental contributions

A few twin studies to date have explored the genetic and environmental contributions to the stability of CU traits in childhood and adolescence. Blonigen et al. (2006) focused on two time-points 7 years apart, when the twins were 17- and 24 years-old. Their results indicate that the heritability of CU traits remained consistent across time and that 58% of the stability of CU traits was due to genetic influences. This finding indicates that the stability in CU traits is substantially influenced by genetic factors. Using the TEDS sample, Fontaine and colleagues (2010) reported that stable high trajectory of CU in childhood (between 7 and 12 years) was strongly heritable in boys (h^2 = .78), but not in girls (h^2 = .00). This finding suggests that, at least in childhood/early adolescence, genetic influences may drive the stability of high levels of CU traits for boys in particular. Forsman et al. (2008) measured CU traits (as well as impulsivity and grandiosity) and examined genetic and environmental contribution to the stability of these traits between ages 16 and 19. The authors focused on a hierarchical model of psychopathic personality in which a higher-order general factor substantially explained the variation in the three psychopathic personality dimensions, both in mid- and late adolescence. Results showed that the observed test-retest correlation of the higher-order psychopathic personality factor was high (r = .60). In addition, as much as 90% of the test-retest correlation was explained by genetic factors.

However, they also found evidence for specific genetic stability in CU. 13% of the unique genetic effects in the CU dimension at age 19 were shared with the corresponding effects at age 16. Thus, their model provides evidence for etiologic generality (together with other aspects of psychopathic personality) and etiologic specificity for the stability of CU traits between mid- and late adolescence. It is of note that, for a subset of children, CU traits are malleable in childhood, either increasing or decreasing with age, rather than remaining persistently high or low (see Fontaine et al., 2010). This is likely to reflect environmental factors interacting with genetic risk to either promote or moderate the development of CU traits, leading to increasing or decreasing CU trajectories respectively (Fontaine et al., 2010). The challenge for researchers and clinicians is to identify the key environmental factors most influential in this regard, and develop interventions that can promote reduction of CU traits thereby reducing the risk of later maladaptive outcomes.

Etiological overlap between CU traits and antisocial behaviour

Twin models have also been important in exploring the etiologic overlap between CU traits and antisocial behaviour. Multivariate genetic models can be used to estimate the extent of genetic/environmental correlation, which refers to the degree of overlap between genetic/environmental influences on different traits or behaviours. A few studies to date have demonstrated a modest to moderate genetic correlation between CU traits and antisocial behaviour when co-variation is measured in the whole population (range of r_g = .16- .57; Bezdijan et al., 2011; Blonigen et al., 2005; Viding et al., 2007). The genetic overlap may be slightly stronger at the extreme high end of both CU and antisocial behaviour distributions (Viding et al. 2007). Larsson et al. (2007) explored the genetic commonality between three psychopathic personality dimensions (grandiose-manipulative, CU, and impulsive- irresponsible dimension) and antisocial behaviour measured at age 13-14 and age 16-17 years. A common genetic factor loaded substantially on both psychopathic personality traits and antisocial behaviour. This was not the case for environmental factors. Forsman et al. (2007) found that externalizing behaviour in childhood (age 8-9) was associated with higher levels of psychopathic personality traits in adolescence (age 13-14) among boys but not in girls. Genetic factors were responsible for this association. Another study by Forsman et al. (2010) showed that psychopathic personality in adolescence (16-17) predicted antisocial behaviour in early

adulthood (19-20), over and above both concurrent and pre-existing levels of antisocial behaviour. The association between adolescent psychopathic personality and adult antisocial behaviour was mainly explained by genetic effects; a result that can be interpreted as a genetically influenced personality-driven process, where individuals are predisposed to higher risk of involvement in antisocial behaviour because of their psychopathic personality. Finally, a recent study by Bezdjian et al. (2011) demonstrated that CU traits shared genetic influences with both reactive and proactive aggression. The genetic correlation was particularly strong between CU traits and proactive aggression (r_g=. 76).

With regard to environmental influences, modest non-shared environmental correlations have been demonstrated between CU traits and antisocial behaviour/aggression (Bezdijan et al. 2011; Viding et al. 2007). This means that although some child specific environmental factors promote the development of both CU and antisocial behaviour/aggression, the child specific environmental influences for the two constructs are largely independent. We recently conducted a longitudinal monozygotic twin differences study to examine negative parental discipline (e.g. shouting and harsh discipline) as a non-shared environmental factor for CU and antisocial behaviour (Viding et al. 2009). Although negative parental discipline at age 7 had a phenotypic association with both CU traits and antisocial behaviour at age 12, negative parental discipline emerged as a non-shared environmental factor for antisocial behaviour alone. In other words those members of the monozygotic twin pair who received more negative parental discipline at age 7 were also more likely to manifest antisocial behaviours at age 12, even after controlling for baseline differences in the level of antisocial behaviour. This was not true for CU traits and we speculated that the phenotypic association between negative parental discipline and CU traits may reflect the genetic endowment within those families with CU+ children, rather than an environmentally driven parenting process that increases risk for CU traits.

Aetiology of antisocial behaviour with and without CU traits

Finally, twin studies have also been helpful in exploring the utility of CU traits as a subtyping factor for individuals with antisocial behaviour. Viding et al. (2005) used information from the TEDS sample, to investigate whether the aetiology of teacher rated antisocial behaviour differs as a function of teacher rated CU at age seven. The authors separated children with elevated

levels of antisocial behaviour (in the top 10% for the TEDS sample) into two groups based on their CU score (in the top 10% or not). Antisocial behaviour in children with CU was under strong genetic influence ($h_g^2 = .81$) and no influence of shared environment. In contrast, antisocial behaviour in children without elevated levels of CU showed moderate genetic influence ($h_g^2 = .30$) and substantial environmental influence ($c_g^2 = .34$, $e_g^2 = .26$). Viding et al. (2008) replicated the finding of different heritability estimates for the AB-HCU and AB-LCU groups using the 9-year teacher data from the TEDS study. In addition, they demonstrated that the strong heritability of antisocial behaviour in the AB-HCU group was not driven by co-occurring hyperactivity.

Molecular genetic studies

Despite the substantial literature demonstrating heritable component of CU traits, we know of only a few published molecular genetic studies of child/adolescent CU traits. The first of these was carried out on a relatively small sample of adolescents with ADHD and reported associations between 'emotional dysfunction' scores of psychopathy (CU) and each of the following allelic variants: the val allele of the cathecol-o-methyl-transferase gene; the low activity allele of monoamine oxidase- A gene (MAOA-L); and the short allele of the serotonin transporter gene (5HTTLPR s) (Fowler et al. 2009). The latter two of these associations were unexpected given that imaging genetic data suggesting that MAOA-L and 5HTTLPR s are associated with heightened amygdala activity to emotional stimuli (e.g. Meyer-Lindenberg et al. 2006; Munafò et al. 2008), in contrast to the reduced amygdala activity to emotional stimuli typically seen in adults with psychopathy and children with AB-HCU (e.g. Birbaumer et al. 2005; Jones et al. 2009; Kiehl et al. 2001; Marsh et al. 2008). It is possible that the findings of Fowler and colleagues are specific to the selected group of adolescents they studied, all of whom had high levels of ADHD symptoms, but relatively low levels of CU traits. A more recent study reported that the long allele of the 5HTTLPR (5HTTLPR l), i.e. the allele conferring low amygdala reactivity, was associated with CU traits in adolescents from low SES backgrounds (Sadeh et al. 2010). This is an extremely interesting finding, as it tentatively suggests that vulnerability to low emotional reactivity may only manifest as high CU traits under disadvantageous socioeconomic conditions. Sadeh et al. (2012) have also reported similar findings in an adult sample of individuals with a forensic/criminal history. Carrying the

5HTTLPR l was associated with the presence of the emotional deficits that characterize the affective factor of psychopathy (i.e. CU traits), however no moderation by environmental variables was found. Sadeh et al. speculated that this may be due to generally high levels of environmental risk in this particular sample, which would allow for the genotype risk to penetrate and appear as genetic main effect. Sadeh et al. (2012) also found that impulsive and irresponsible lifestyle features of psychopathy were higher among low-activity than high-activity MAO-A carriers.

Two recent studies have also looked at the role of the oxytocin and oxytocin receptor gene variants in relation to CU traits and childhood-onset aggression (Beitchman et al. 2012; Malik et al. 2012). Oxytocin is thought to play an important role in various social behaviours. For example, it has been shown to amplify attachment, human bonding and trust, whilst its dysregulation has been associated with increased aggression (Campbell 2010). Beitchman et al. (2012) genotyped six single-nucleotide polymorphisms (SNPs) in the oxytocin (20p12) and oxytocin receptor genes (3p25) and found that those with the AA genotype of the oxytocin receptor SNP rs237885had significantly higher CU traits than AC or CC genotype carriers. However, when the same group inspected different oxytocin and oxytocin receptor SNPs, no association with CU traits was found (Malik et al., 2012). Findings with regard to oxytocin genes therefore need replication and refinement.

Finally, new technologies, such as DNA pooling are enabling genome-wide association studies that search for novel single nucleotide polymorphisms (SNPs), which may be associated with AB-HCU. DNA pooling refers to a genetic screening method that combines DNA from many individuals in a single molecular genetic analysis to generate a representation of allele frequencies. A DNA pool can thus be generated for all cases and all controls and allele frequencies can be compared between these pools. We recently conducted such a study and although no SNPs reached genome-wide significance, there were some potential candidates near neurodevelopmental genes, including ROBO2 (Viding et al. 2010). The association with ROBO2 has been recently replicated in an independent sample, although it appears that the association concerns antisocial behaviour in general, rather than CU specifically (Dadds et al. in press).

Findings from the genetic studies could be fruitfully incorporated into imaging genetic investigations of psychopathy. We have recently used twin design to document that aberrant structural brain development in AB-HCUAB-HCU reflects genetic, rather than environmental vulnerability to this behavioural outcome (Rijsdijsk et al. 2010). Investigations with specific genotypes are still pending.

Summary – Genetic Research

Numerous twin studies from different laboratories suggest that both individual and group differences in CU traits are moderately to strongly heritable. Child specific (non-shared) environmental factors are also important in accounting for individual and group differences in CU traits. However, environmental factors that make children growing up in the same family similar to each other (termed shared environmental factors in twin models) do not typically play a role in individual and group differences in CU traits. Girls with stable high CU traits represent a possible exception, as shared environmental factors appear to be important for the development of CU traits in this group.

Twin studies can go beyond answering questions about relative importance of heritable and environmental influences. To date, such studies have advanced our knowledge about CU traits in several important ways. First, they have demonstrated that stability of CU traits is typically driven by genetic influences (particularly in boys), but also that there is substantial environmental influence that may serve to increase or moderate levels of CU over time, thereby contributing to an increasing or decreasing trajectory of CU trait development. Third, a monozygotic twin differences data suggest that negative parental practices do not act as a child specific environmental risk factor for CU, but may instead reflect genetic vulnerability within families. However, aspects of positive parenting are yet to be investigated within this framework and may be a promising environmental modulator of CU traits. Fourth, a number of studies have shown that CU and antisocial behaviour share a degree of genetic risk and (to a modest extent) child specific environmental risk factors. Finally, antisocial behaviour in the presence (but not in the absence) of CU traits appears strongly heritable, suggesting that CU traits are a useful subtyping index for children with disruptive behaviours.

Research into specific polymorphisms that increase risk of CU traits or AB-HCU is still in its infancy and only a handful of studies have been conducted to date. It is too early to draw firm conclusions from the existing, meagre evidence base, although there are promising leads with regard to genotypes that predispose to low emotional reactivity, as well as those that may affect early neurodevelopment.

Neural correlates of CU traits

Functional Magnetic Resonance Imaging studies

Children with AB-HCU share an affective profile with adult psychopaths showing reduced sensitivity to visual or vocal displays of distress emotions and poor modulation of behaviour in response to punishment (Blair & Viding, 2008). In line with the behavioural and experimental neuropsychology data, fMRI findings for children with AB-HCU indicate functional deficits consistent with low emotional responsiveness to others' distress and poor ability to learn from reinforcement information. Aberrant neural functioning (as compared with typically developing children or children with ADHD) has been observed for children with AB-HCU in the amygdala, ventromedial prefrontal cortex (vmPFC), orbitofrontal cortex (OFC), anterior insula and caudate; brain areas that are involved in processing basic emotional salience, reinforcement learning, and emotion regulation.

Recent studies have reported reduced amygdala activity in children with AB-HCU as compared with typically developing children or children with ADHD (Jones et al. 2009; Marsh et al. 2011a; Marsh et al. 2008; Sebastian et al. 2012; Viding et al. 2012; White et al. 2012). Children with AB-HCU show reduced amygdala response to other's distress (e.g. Jones et al. 2009; Marsh et al. 2008; White et al. 2012) and reduced functional coupling between amygdala and OFC when viewing fearful facial expressions (Marsh et al. 2008). Reduced amygdala activity in children with AB-HCU also seems to extend to more complex forms of social cognition, such as categorisation of legal and illegal behaviours in a moral judgment task (Marsh et al. 2011a) or affective theory of mind judgements (Sebastian et al. 2012). Furthermore, CU traits and conduct problems also seem to present differential contributions to amygdala activity in children with AB (Sebastian et al. 2012; Viding et al. 2012). Viding, Sebastian et al. (2012) have demonstrated a

differential amygdala activity pattern to preattentively presented fear across the spectrum of CU traits in children with AB. In this study, boys with AB-HCU compared with AB-LCU presented significantly lower amygdala activity to backwardly masked fearful versus calm faces, whilst amygdala activity level in typical developing boys was intermediate between those of the conduct problems groups. These findings not only indicate that reduced amygdala activation to salient stimuli in children with AB-HCU encompasses even early stages of information processing, but also suggest an affective processing deficit specific to this group. White et al (2012) have also demonstrated that reduced amygdala reactivity in response to fearful faces was associated with CU, but not with other traits commonly associated with AB such as impulsivity. A recent study from our group (Sebastian et al. 2012) have shown that the unique variance associated with CU traits was related to decreased amygdala activity, while unique variance associated with conduct problems was associated with increased amygdala activity to emotionally salient social scenes. These results clearly suggest that reduced amygdala activation as characteristic of the AB-HCU subgroup rather than of children with conduct problems more generally.

Abnormal vmPFC and OFC response to punishment and reward in adolescents with AB-HCU have also been reported (Finger et al. 2011; Finger et al. 2008). In one study, participants had to choose the 'correct' stimulus from a pair of items. From time to time the reinforcement associations reversed and a previously rewarded stimulus became unrewarded, while the previously unrewarded stimuli became rewarded. Finger et al. (2008) reported that typically developing children and children with ADHD showed a reduction in vmPFC activity following an unexpected punishment. Such reduction in vmPFC activity has been shown to co-occur with prediction error (Mitchell 2011). In contrast, youth with AB-HCU did not show this reduction in vmPFC activity. In another study, using a passive avoidance paradigm where participants had to learn which stimuli were 'good' (rewarded) and which were 'bad' (unrewarded), Finger et al. (2011) also demonstrated that children with AB-HCU showed less OFC and caudate responsiveness to early stimulus-reinforcement exposure, and less OFC responsiveness to rewards. These neural differences are likely to index compromised sensitivity to early reinforcement information in the OFC and caudate and compromised sensitivity to reward outcome information in the OFC in adolescents with AB-HCU. These fMRI findings in AB-

HCU are in line with those typically reported in studies of adult psychopaths (e.g. Birbaumer et al. 2005; Kiehl et al. 2001) and suggest functional neural bases for why individuals with AB-HCU appear unaffected by other people's distress and often make and repeat disadvantageous decisions.

Structural magnetic resonance imaging studies

To date there have been only two studies that report on structural MRI correlates of AB-HCU in children. De Brito et al. (2009) found that compared with typically developing boys, boys with AB-HCU had increased grey matter concentration (GMC), in several brain areas implicated in decision-making, moral processing, and self-reflection. These included OFC, insula, anterior cingulate cortex (ACC), posterior cingulate cortex (PCC), and superior temporal cortex. Subsequently, De Brito et al. (2011) showed that compared with typically developing boys, those with AB-HCU exhibited *decreased* white matter concentration (WMC) in a subset of the brain areas where increased GMC was found for boys with AB-HCU, including ACC and superior temporal cortex. These findings indicate that children with AB-HCU are characterized by atypical neural structure in many of the same areas where grey and white matter abnormalities have also been reported in adults with psychopathy (Gao et al. 2009; Yang and Raine 2009). However, somewhat puzzlingly the direction of the effect (at least for grey matter) is different in the child, as compared with adult studies. It is of note that De Brito et al. (2009; 2011) studied children who were between 10-13 years of age. Recent brain imaging evidence in normative samples suggests that grey matter decreases and white matter increases in several of the brain areas implicated in AB-HCU during this period of early adolescence (Gogtay et al., 2004). This is contrary to the pattern observed for the 10-13 year old boys with AB-HCU, possibly indicative of aberrant brain maturation for this group in early adolescence. More recently, Sumich et al. (2012) have found that AB-HCU boys do not show the typical maturational pattern of decline in the event-related potential component N200 amplitude in midline frontal and temporal electrodes, further evidencing a possible atypical maturation for this group of boys. These data are not necessarily at odds with the findings from adult studies, which clearly represent a very different developmental stage. Distinct developmental disorders can follow markedly different patterns of structural brain development (Shaw et al. 2010) and future longitudinal studies should probe the exact developmental pattern characteristic of AB-HCU.

A number of functional and structural MRI studies have focused on children with antisocial behaviour without subtyping on CU traits (e.g. see reviews of Sterzer and Stadler 2010 and Rubia 2011; see also Passamonti et al. 2010; Rubia et al. 2009; Fairchild et al. 2011), but these are difficult to interpret in the context of AB-HCU as the relative composition of those individuals who are high vs. low on CU traits is unclear. Furthermore, the stimuli used in different fMRI studies varies substantially and across functional studies, and the possible suppressor effects between conduct problems and CU, which are known to occur at both the behavioural (e.g. Frick et al. 1999; Hicks and Patrick 2006) and neural levels (Sebastian et al. 2012), have not been assessed.

Summary – Magnetic Resonance Imaging research

The sparse magnetic resonance imaging evidence base suggests that AB-HCU is associated with atypical patterns of brain structure and function, particularly in the areas critical for affective processing, affective decision-making, and moral emotions. The findings are broadly in line with those reported in studies of adult psychopaths and suggest neural bases for the types of traits and behaviours associated with AB-HCU. Specifically, children with AB-HCU show lower amygdala reactivity to fearful faces than typically developing children or children with ADHD. They also show abnormal activity in vmPFC, OFC, and caudate; these are areas associated with prediction error and monitoring of reward outcomes during affective decision-making and reversal learning.

Integrating genetic and neuroimaging findings

Genetic vulnerability to HCU may contribute to some of the neural vulnerabilities characteristic of AB-HCU and integration of genetic and neuroimaging approaches may yield novel information important for understanding the development of psychopathy. We recently conducted a twin study that investigated whether GMC on those areas that differentiated children with AB-HCU from typically developing children were heritable (Rijsdijsk et al. 2010). We also investigated whether common genetic influences were important for GMC and AB-HCU status

and whether such common genetic influences were responsible for the phenotypic association between higher GMC and AB-HCU. Of the brain areas that showed group differences and heritable influences, left PCC, right dACC shared a moderate degree of genetic influences with AB-HCU. These common genetic influences were entirely responsible for the phenotypic association between GMC and AB-HCU. These findings provide preliminary evidence that left PCC and right dACC may constitute intermediate phenotypes for the development of psychopathy. Both left PCC and right dACC are involved in empathy for pain, moral judgments, and self-referential thinking (including judgments and obligations) and as such represent logical intermediate phenotype markers for the development psychopathy. It is premature to speculate regarding the putative mechanism by which genes could increase GMC and in turn lead to increased levels of AB-HCU. However, future imaging genetic studies could investigate the role of specific neurodevelopmental genes in explaining GMC differences between AB-HCU and typically developing children. It is also of interest to investigate genetic contributions to functional brain differences using both twin and candidate gene imaging approaches. For example, it would be important to explore the role of 5HTLPPR in modulating neural activity to emotional stimuli in children with high levels of CU traits and different levels of social adversity.

Treatment Implications

Conceptually, children with AB-HCU would be hypothesised to respond differentially to treatment (as compared with AB-LCU) given their distinct pattern of etiological and neurocognitive vulnerability. For example, we have considered evidence that these children have genetic vulnerability to antisocial behaviour and show functional and structural neural abnormalities that may predispose them to deviant development of emotion processing, reinforcement learning and empathy. Only relatively recently have studies begun to examine how treatment outcome might vary in relation to a child's level of CU traits, and whether the efficacy of treatment strategies vary depending on level of CU traits.

Several parenting studies by Mark Dadds, David Hawes and colleagues have provided preliminary evidence for two conclusions regarding the nature of CU traits in preadolescent children. *Firstly, children with high levels of CU traits appear to respond less well to some*

typical parenting interventions. Following a 10-week standardized parenting programme for children aged 3 to 8 years of age with conduct problems it was found that high CU traits uniquely predicted poor response to treatment, even after controlling for family characteristics (Hawes and Dadds 2005). Observational data relating to the parent-child interactions in the home indicated that HCU children differed only in their response to the 'time-out' procedure. This suggests differential responsiveness to a traditional treatment component, consistent with the evidence from the experimental literature that these children may be relatively punishment insensitive (Frick and Viding 2009). *Secondly, high levels of CU traits appear malleable in a subset of children.* In a subsequent study Hawes and Dadds (2007) examined the malleability and stability of CU traits in this sample including at 6-month follow-up. They found that CU scores in a subset of the sample dropped significantly following treatment. While this change may reflect problems of measuring CU traits accurately (e.g. parents over-reporting these traits at presentation), it seems likely that the effect is consistent with a genuine malleability of CU traits in some children. This finding is in line with that reported for older preadolescent children (Pardini et al. 2007). A sample of 120 aggressive children in the fifth grade were followed over a one-year period; those exposed to lower levels of physical punishment and reporting greater levels of parental warmth and involvement showed decreases in CU traits over time. *Thirdly, while coercive parenting seems to particularly exacerbate conduct problems in boys with low levels of CU traits, parental warmth appears to particularly ameliorate conduct problems in boys with high levels of CU traits* (Pasalich et al. 2011). In this study of 95 clinic referred boys aged 2-12 years, Pasalich et al. used direct observations of family interaction and a Five-Minute Speech Sample (rather than questionnaires) to measure coercive parenting and parental warmth respectively. These findings add empirical weight to existing evidence that parental warmth and involvement is associated with changes in levels of CU traits over time (Pardini et al. 2007). In particular, they suggest that the affective quality of the parent-child relationship (as opposed to discipline) is more important for the socialisation of under-aroused children who have blunted emotional responses by virtue of their high CU traits (Kochanska 1997; Pasalich et al. 2011). How to effectively promote the affective quality of the parent-child relationship should be at the forefront of studies focusing on improvement of treatment efficacy.

These findings are at least suggestive that parenting practices, which are amenable to change through intervention, may influence levels of CU traits over time. However, the nature of any relationship between parenting and CU traits is likely to be complex and may involve bidirectional influences. A recent study by Hawes et al. (2011) examined the relationship between CU traits and parenting in a large community sample of children aged between 3 and 10 years of age. CU traits predicted change in relation to inconsistent discipline, corporal punishment and parental involvement with the latter two factors moderated by child age and sex. It is possible, therefore, that to some degree CU traits may serve to elicit escalating levels of harsh and inconsistent discipline by parents; however, it remains possible that child driven effects on negative parenting are primarily attributable to conduct problems, and not CU traits (Larsson et al. 2008; Pasalich et al. 2011).

A separate line of research that may have treatment implications has investigated the atypical pattern of eye gaze and eye contact in children with high CU traits. As outlined earlier in this paper, children with high levels of CU traits have deficits in fear recognition and do not automatically orient to eye-region of the face (Dadds et al. 2006; Frick and Viding 2009; Sylvers et al. 2011). However, when these children were asked to 'look at the eyes' of the stimulus faces, the recognition deficits disappeared (Dadds et al. 2006; Dadds and Rhodes 2008). It has also been shown that children, aged between 5 and 15 years of age with high CU traits show consistent impairments in their eye contact with their parents (Dadds et al. 2011). This finding has been replicated in a younger sample in a task requiring a 'loving' interaction between the child and their mother (Dadds, et al., 2011). Understanding deficits in these domains is potentially critical to intervention in two ways. Firstly, deficits in basic social interaction processes may be relevant in informing targets for parenting and child-based interventions. Secondly, given that most psychologically based intervention relies on establishing an effective therapeutic alliance it will be important to reconsider traditional approaches to establishing rapport when engaging therapeutically with children with high CU traits. In a recent study, Dadds et al. (Dadds et al. 2012) report the findings of randomised control trial of emotion recognition training (ERT) versus treatment as usual in a group of children (n=195) referred for a range of behavioural and emotional problems. While ERT did not have an effect on the group as a whole, children with higher levels of CU traits (even those without a diagnosis of conduct

disorder) showed more improvement in affective empathy and reduced conduct problems in response to ERT. Strikingly, ERT served to reduce level of conduct problems compared to baseline in children with high CU traits, while TAU (treatment-as-usual) was associated with an increase in conduct problems in this group. These preliminary findings serve to underscore the heterogeneous nature of treatment response in children presenting with conduct problems and provides a promising basis to develop tailored treatment strategies for children with higher levels of CU traits.

Increasingly, behavioural interventions are also being delivered in school settings (Viding et al. 2011). Given that children with AB-HCU often come from families characterised by multiple difficulties (where parents are also likely to have genetic and neurocognitive vulnerabilities), school settings may provide an important context for delivering consistent intervention. One of the most commonly studied problem behaviours in school setting is bullying, and both CU traits and a combination of CU traits and antisocial behaviour are associated with increased rates of bullying behaviour (e.g. Crapanzano et al. 2011; Muñoz et al. 2011; Viding et al. 2009). Neuroscience findings (e.g. Finger et al. 2011; Marsh et al. 2008; Sebastian et al. 2012) indicate there is a growing case for developing tailored approaches to reduce bullying behaviour in children with AB-HCU because they are unlikely to be well served by the most commonly implemented approaches (Smith et al. 2004). For example, educative approaches often aim to elicit empathy in the bully and focus on the distress they cause other children as a means to engender in them a motivation to change. The second commonly used intervention approach, exemplified by 'zero-tolerance' policies, is essentially punitive and involves exclusion from school and other high-level disciplinary sanctions. The research we have reviewed above indicates that neither of the above approaches is likely to work as effectively in children with callous-unemotional conduct problems because they have difficulties empathising and are less responsive to punishment. A more successful approach could involve, for example, the establishment of a system of rewards for behaviour incompatible with bullying; in parallel there would be a need to ensure that rewards for bullying behaviour (e.g. gaining peer dominance, status and goods) were minimized, for example through close supervision by adults or peer mentors. Currently, however, schools rarely implement systemic and peer-supported approaches to bullying (Sherer and Nickerson 2010).

Genetic and neuroscience research is helping to inform a model of developmental vulnerability to adult psychopathy. Although this research suggests that children with high CU traits or AB-HCU are genetically and neurocognitively vulnerable, existing research also strongly endorses that CU traits are malleable during childhood. Longitudinal, genetically informative data suggests that environmental influences account for a substantial proportion of variance in CU traits and are also important for change in these traits. Phenotypic data has demonstrated that positive parenting and parental involvement can reduce CU traits over time (Hawes et al. 2011). These data are in line with the notion that despite genetic risk for AB-HCU (or later psychopathy), there are no genes that directly code for psychopathic behaviour. Genes code for proteins that influence characteristics such as neurocognitive vulnerabilities that may in turn increase risk for developing psychopathy. This risk may only manifest itself under unfavourable environmental circumstances and genetic variants implicated in CU and AB-HCU are likely to confer advantages, as well as disadvantages, depending on the environmental context.

A particularly important implication from the neuroscience research is that interventions for children with AB-HCU may need to be tailored such that they take into account their distinct pattern of neurocognitive vulnerability. Specifically, it may be fruitful to avoid punishment-oriented or explicit empathy induction strategies. Preliminary evidence from behavioural and treatment studies suggests that enhancing positive parenting and parental involvement, as well as applying consistent rewards may represent promising foci for future treatment research.

Future agenda

Aetiology of CU traits

Genetic research is likely to advance greatly in the coming decade, including novel epigenetic approaches that may help us uncover mechanisms of gene-environment interaction or studies of rare copy number variants that may affect smaller subsets of individuals at risk for developing psychopathy. It is useful to consider the following pointers with regard to current, but in

particular future molecular genetic investigations. *First, there are no genes for psychopathy*. Genes code for proteins that influence characteristics such as neurocognitive vulnerabilities that may in turn increase risk for developing psychopathy. *Second, genetic risk for psychopathy may only manifest itself under unfavourable environmental circumstances* (e.g. Sadeh et al. 2010) and genetic variants implicated in CU and AB-HCU are likely to include several common polymorphisms that confer advantages, as well as disadvantages, depending on the environmental context. *Third, we know that the neurocognitive vulnerabilities associated with psychopathy (or risk for development of psychopathy) are at least partially distinct from those associated with antisocial behaviour in general.* This suggests that the risk alleles for psychopathy may not be the same as risk alleles as those for antisocial behaviour in the absence of CU traits. (See Glenn (2010) for a review of this in relation to 5-HTTLPR and Viding and Jones (2008) for a more general proposal of differential genetic vulnerability in AB-HCU and AB-LCU). The study by Sadeh et al. (2010) is in line with this possibility, as it demonstrated not only that the long allele of the 5-HTTLPR predisposed individuals to CU traits in low SES environments, but also that the short allele of the same gene predisposed individuals to impulsive antisocial behaviour. Buckholtz and Meyer-Lindenberg (2008) have also speculated that MAOA-L allele, which has received a lot of attention as a risk allele for antisocial behaviour, may predispose to threat reactive and impulsive, rather than psychopathic antisocial behaviour. The MAOA-L genotype is associated with a pattern of hyper-reactivity of emotion processing areas of the brain (Meyer-Lindenberg et al. 2006), which is in direct contrast to the pattern typically reported for individuals with psychopathy (e.g. Birbaumer et al. 2005; Kiehl et al. 2001). It is interesting to note that some studies have reported increased vulnerability to antisocial behaviour in the presence of the MAOA-H allele (e.g. Manuck et al. 2000). These may reflect false positive findings, but could also reflect the relative composition of HCU and LCU individuals in different studies

Neural Correlates of CU traits

Unfortunately only one of the neuroimaging studies to date have involved an explicit comparison of children with AB-HCU and AB-LCU (Viding et al. 2012) and only one other study has

examined the independent contributions of AB and CU to neural activity (Sebastian et al. 2012). Such studies are clearly needed in the future.

In addition, extant studies have only utilised a limited number of paradigms. To date these have included: simple gender decision task when viewing facial stimuli of emotional and neutral content; passive avoidance learning; reversal learning, affective and non-affective theory of mind cartoons, and categorisation of legal and illegal behaviours. In the future it would be of interest to investigate neural responses in children with AB-HCU to stimuli related to empathy, morality and emotion regulation. It would also be of interest to assess functional and structural brain development longitudinally, including the identification of possible 'brain biomarkers' that might predict future behavioural outcomes. Combining imaging methodologies, with genotyping and study of environmental risk is similarly likely to prove informative, particularly as we try to understand multifinality of outcomes for children with AB-HCU. Although this group of children are at an increased risk of developing psychopathy, not all of them do so. By combining different levels of analyses longitudinally we will be able to develop an integrated model of AB and its relation to CU traits that can better inform approaches to prevention and intervention.

Development of psychopathy: Where do we go from here?

Integrating information across multiple levels of analyses and combining different methodologies within a single study, while keeping in mind multiple possible developmental pathways to antisocial behaviour (equifinality) and different possible outcomes following childhood CU traits (multifinality) (Cicchetti and Rogosch 1996) is important if the field of developmental psychopathology in general is to advance. In relation to psychopathy this approach is already bearing fruit (Blair and Viding 2008; Frick and Viding 2009). The current evidence base suggests that AB is associated with a number of different developmental trajectories, consistent with the notion of equifinality. Different etiological pathways can lead to high levels of antisocial behaviour; as we have seen children with AB-HCU appear to be the most genetically vulnerable to persistent antisocial behavioural problems and in some cases psychopathy. However, the current data also clearly indicate that there are no genes for antisocial

behaviour or psychopathy, not even in this group with a stronger genetic predisposition. Rather, variation in genes is likely to code for variation in information/affective processing styles. The information processing style of children with AB-HCU is characterised by low emotional reactivity to others' distress and difficulty in learning from sanctions. We have also reviewed neuroimaging evidence that this group of children show related atypical patterns of neural function and structure. Yet these patterns are unlikely to be fixed and determinate. Multifinality characterises outcomes for children with AB-HCU as with all children showing antisocial behaviour. For example, twin studies suggest that environmental factors can influence both the level of CU traits and of antisocial behaviour. Data from clinic and community studies is consistent with this notion with preliminary data indicating that these children with AB-HCU may be particularly responsive to warm parenting practices and reward based strategies.

In light of the fact that neurobiological research on CU traits and AB-HCU is in its infancy, several important questions remain outstanding. *Firstly, what genes are involved in vulnerability to AB-HCU?* In the coming years we are likely to discover that some of the polymorphisms we thought were important may simply represent false positive finding and others, which at first sight appeared less intuitive, may represent true genetic risk. *Secondly, are genetic or neural biomarkers predictive of long-term outcome and treatment response?* Because our diagnostics systems are based on behavioural criteria, we can comfortably predict that there will not be a single basis to any given disorder (genetic or otherwise); but we may be able to isolate specific biomarkers that can provide clues to developmental risk. *Finally, how do both genetic and environmental risk factors pertinent for psychopathy manifest at the neural level across development?* Currently most research has been cross-sectional in nature. We need a much better picture of how atypical patterns of neural function develop over time in children with AB-HCU if we are to tease apart which effects reflect developmental immaturity or delay, and which reflect an abnormal pattern of development. Addressing these questions effectively represents a challenge to basic science research, but further advances in this field will help us better understand how risk factors in childhood may lead to the development of psychopathy in adulthood. We believe that a better delineation of (even putative) causal mechanisms has the potential to inform more effective approaches to prevention and treatment for at-risk children.

REFERENCES

Barker ED, Oliver BR, Viding E, Salekin RT, Maughan B (2011) The impact of prenatal maternal risk, fearless temperament and early parenting on adolescent callous-unemotional traits: A 14-year longitudinal investigation. Journal of Child Psychology and Psychiatry and Allied Disciplines 52 (8):878-888.

Beitchman JH, Zai CC, Muir K, Berall L, Nowrouzi B, Choi E, Kennedy JL (2012) Childhood aggression, callous-unemotional traits and oxytocin genes. European Child and Adolescent Psychiatry 21 (3):125-132.

Bezdjian S, Raine A, Baker LA, Lynam DR (2011) Psychopathic personality in children: Genetic and environmental contributions. Psychological Medicine 41 (3):589-600.

Birbaumer N, Veit R, Lotze M, Erb M, Hermann C, Grodd W, Flor H (2005) Deficient fear conditioning in psychopathy: A functional magnetic resonance imaging study. Archives of General Psychiatry 62 (7):799-805.

Blair RJR, Viding E (2008) Psychopathy. Rutter's Child and Adolescent Psychiatry:852-863

Blonigen DM, Carlson SR, Krueger RF, Patrick CJ (2003) A twin study of self-reported psychopathic personality traits. Personality and Individual Differences 35 (1):179-197.

Blonigen DM, Hicks BM, Krueger RF, Patrick CJ, Iacono WG (2005) Psychopathic personality traits: Heritability and genetic overlap with internalizing and externalizing psychopathology. Psychological Medicine 35 (5):637-648.

Blonigen DM, Hicks BM, Krueger RF, Patrick CJ, Iacono WG (2006) Continuity and change in psychopathic traits as measured via normal-range personality: A longitudinal-biometric study. Journal of Abnormal Psychology 115 (1):85-95.

Bouchard Jr TJ, Loehlin JC (2001) Genes, evolution, and personality. Behavior Genetics 31 (3):243-273.

Bowlby J (1946) Forty-four juvenile thieves: Their home life. London: Bailliere, Tindall & Cox.

Buckholtz JW, Meyer-Lindenberg A (2008) MAOA and the neurogenetic architecture of human aggression. Trends in Neurosciences 31 (3):120-129.

Campbell A (2010) Oxytocin and human social behavior. Personality and Social Psychology Review 14 (3):281-295.

Cicchetti D, Rogosch FA (1996) Equifinality and multifinality in developmental psychopathology. Development and Psychopathology 8 (4):597-600.

Cleckley H (1941). The mask of insanity (1 ed.). St Louis, MO: Mosby.

Crapanzano AM, Frick PJ, Childs K, Terranova AM (2011) Gender Differences in the Assessment, Stability, and Correlates to Bullying Roles in Middle School Children. Behavioral Sciences and the Law 29 (5):677-694.

Dadds MR, Cauchi AJ, Wimalaweera S, Hawes DJ, Brennan J (2012) Outcomes, moderators, and mediators of empathic-emotion recognition training for complex conduct problems in childhood. Psychiatry Research 199 (3):201-207.

Dadds MR, Jambrak J, Pasalich D, Hawes DJ, Brennan J (2011) Impaired attention to the eyes of attachment figures and the developmental origins of psychopathy. Journal of Child Psychology and Psychiatry and Allied Disciplines 52 (3):238-245.

Dadds MR, Moul C, Cauchi A, Hawes DJ, Brennan J (in press) Replication of a ROBO2 polymorphism associated with conduct problems but not psychopathic tendencies in children. Psychiatric Genetics.

Dadds MR, Perry Y, Hawes DJ, Merz S, Riddell AC, Haines DJ, Solak E, Abeygunawardane AI (2006) Attention to the eyes and fear-recognition deficits in child psychopathy. British Journal of Psychiatry 189 (SEP.):280-281.

Dadds MR, Rhodes T (2008) Aggression in young children with concurrent callous-unemotional traits: Can the neurosciences inform progress and innovation in treatment approaches? Philosophical Transactions of the Royal Society B: Biological Sciences 363 (1503):2567-2576.

De Brito SA, Mechelli A, Wilke M, Laurens KR, Jones AP, Barker GJ, Hodgins S, Viding E (2009) Size matters: Increased grey matter in boys with conduct problems and callousunemotional traits. Brain 132 (4):843-852.

De Brito SA, McCrory EJ, Mechelli A, Wilke M, Jones AP, Hodgins S, Viding E (2009) Small, but not perfectly formed: Decreased white matter concentration in boys with psychopathic tendencies. Molecular Psychiatry 16 476-477.

De Wied M, Van Boxtel A, Matthys W, Meeus W (2012) Verbal, facial and autonomic responses to empathy-eliciting film clips by disruptive male adolescents with high versus low callous-unemotional traits. Journal of Abnormal Child Psychology 40 (2):211-223.

Dodge KA, Crick NR (1990) Social Information-Processing Bases of Aggressive Behavior in Children. Personality and Social Psychology Bulletin 16 (1):8-22.

Fairchild G, Passamonti L, Hurford G, Hagan CC, Von Dem Hagen EAH, Van Goozen SHM, Goodyer IM, Calder AJ (2011) Brain structure abnormalities in early-onset and adolescent-onset conduct disorder. American Journal of Psychiatry 168 (6):624-633.

Finger EC, Marsh AA, Blair KS, Reid ME, Sims C, Ng P, Pine DS, Blair RJR (2011) Disrupted reinforcement signaling in the orbitofrontal cortex and caudate in youths with conduct

disorder or oppositional defiant disorder and a high level of psychopathic traits. American Journal of Psychiatry 168 (2):152-162.

Finger EC, Marsh AA, Mitchell DG, Reid ME, Sims C, Budhani S, Kosson DS, Chen G, Towbin KE, Leibenluft E, Pine DS, Blair JR (2008) Abnormal ventromedial prefrontal cortex function in children with psychopathic traits during reversal learning. Archives of General Psychiatry 65 (5):586-594.

Fontaine NMG, McCrory EJP, Boivin M, Moffitt TE, Viding E (2011) Predictors and Outcomes of Joint Trajectories of Callous-Unemotional Traits and Conduct Problems in Childhood. Journal of Abnormal Psychology 120 (3):730-742.

Fontaine NMG, Rijsdijk FV, McCrory EJP, Viding E (2010) Etiology of different developmental trajectories of callous-unemotional traits. Journal of the American Academy of Child and Adolescent Psychiatry 49 (7):656-664.

Forsman M, Larrson H, Andershed H, Lichtenstein P (2007) Persistent disruptive childhood behavior and psychopathic personality in adolescence: A twin study. British Journal of Developmental Psychology 25 383-398.

Forsman M, Lichtenstein P, Andershed H, Larsson H (2008) Genetic Effects Explain the Stability of Psychopathic Personality From Mid- to Late Adolescence. Journal of Abnormal Psychology 117 (3):606-617.

Forsman M, Lichtenstein P, Andershed H, Larsson H (2010) A longitudinal twin study of the direction of effects between psychopathic personality and antisocial behaviour. Journal of Child Psychology and Psychiatry and Allied Disciplines 51 (1):39-47.

Fowler T, Langley K, Rice F, Van Den Bree MBM, Ross K, Wilkinson LS, Owen MJ, O'Donovan MC, Thapar A (2009) Psychopathy trait scores in adolescents with childhood ADHD: The contribution of genotypes affecting MAOA, 5HTT and COMT activity. Psychiatric Genetics 19 (6):312-319.

Frick PJ, Cornell AH, Barry CT, Bodin SD, Dane HE (2003) Callous-unemotional traits and conduct problems in the prediction of conduct problem severity, aggression, and self-report of delinquency. Journal of Abnormal Child Psychology 31 (4):457-470.

Frick PJ, Lilienfeld SO, Ellis M, Loney B, Silverthorn P (1999) The association between anxiety and psychopathy dimensions in children. Journal of Abnormal Child Psychology 27 (5):383-392

Frick PJ, Moffitt TE (2010) A proposal to the DSM-V childhood disorders and the ADHD and disruptive behavior disorders work groups to include a specifier to the diagnosis of conduct disorder based on the presence of callous-unemotional traits. American Psychiatric Association:1-36

Frick PJ, O'Brien BS, Wootton JM, McBurnett K (1994) Psychopathy and conduct problems in children. Journal of Abnormal Psychology 103 (4):700-707.

Frick PJ, Viding E (2009) Antisocial behavior from a developmental psychopathology perspective. Development and Psychopathology 21 (4):1111-1131.

Gao Y, Glenn AL, Schug RA, Yang Y, Raine A (2009) The neurobiology of psychopathy: A neurodevelopmental perspective. Canadian Journal of Psychiatry 54 (12):813-823

Glenn AL (2011) The other allele: Exploring the long allele of the serotonin transporter gene as a potential risk factor for psychopathy: A review of the parallels in findings. Neuroscience and Biobehavioral Reviews 35 (3):612-620.

Gogtay N, Giedd JN, Lusk L, Hayashi KM,, Greenstein D, Vaituziz AC, Nugent III TF, Herman DH, Clasen LS, Toga AW, Rapoport JL, Thompson PM (2004) Dynamic mapping of human cortical development during childhood through early adulthood. Proceedings of National Academy of Science 101 8174-8179.

Hawes DJ, Dadds MR (2005) The treatment of conduct problems in children with callous-unemotional traits. Journal of Consulting and Clinical Psychology 73 (4):737-741.

Hawes DJ, Dadds MR (2007) Stability and malleability of callous-unemotional traits during treatment for childhood conduct problems. Journal of Clinical Child and Adolescent Psychology 36 (3):347-355

Hawes DJ, Dadds MR, Frost ADJ, Hasking PA (2011) Do childhood callous-unemotional traits drive change in parenting practices? Journal of Clinical Child and Adolescent Psychology 40 (4):507-518.

Hicks BM, Patrick CJ (2006) Psychopathy and negative emotionality: Analyses of suppressor effects reveal distinct relations with emotional distress, fearfulness, and anger-hostility. Journal of Abnormal Psychology 115 (2):276-287.

Jones AP, Happé FG, Gilbert F, Burnett S, Viding E (2010) Feeling, caring, knowing: different types of empathy deficit in boys with psychopathic tendencies and autism spectrum disorder. Journal of Child Psychology and Psychiatry, and Allied Disciplines 51 (11):1188-1197

Jones AP, Laurens KR, Herba CM, Barker GJ, Viding E (2009) Amygdala hypoactivity to fearful faces in boys with conduct problems and callous-unemotional traits. American Journal of Psychiatry 166 (1):95-102.

Kiehl KA, Smith AM, Hare RD, Mendrek A, Forster BB, Brink J, Liddle PF (2001) Limbic abnormalities in affective processing by criminal psychopaths as revealed by functional magnetic resonance imaging. Biological Psychiatry 50 (9):677-684.

Kim-Cohen J, Caspi A, Moffitt TE, Harrington H, Milne BJ, Poulton R (2003) Prior juvenile diagnoses in adults with mental disorder: Developmental follow-back of a prospective-longitudinal cohort. Archives of General Psychiatry 60 (7):709-717.

Kochanska G (1997) Mutually Responsive Orientation between Mothers and Their Young Children: Implications for Early Socialization. Child Development 68 (1):94-112

Kumsta R, Sonuga-Barke E, Rutter M (2012) Adolescent callous-unemotional traits and conduct disorder in adoptees exposed to severe early deprivation. British Journal of Psychiatry 200 (3):197-201.

Larsson H, Andershed H, Lichtenstein P (2006) A genetic factor explains most of the variation in the psychopathic personality. Journal of Abnormal Psychology 115 (2):221-230.

Larsson H, Tuvblad C, Rijsdijk FV, Andershed H, Grann M, Lichtenstein P (2007) A common genetic factor explains the association between psychopathic personality and antisocial behavior. Psychological Medicine 37 (1):15-26.

Larsson H, Viding E, Plomin R (2008) Callous-unemotional traits and antisocial behavior: Genetic, environmental, and early parenting characteristics. Criminal Justice and Behavior 35 (2):197-211.

Lau KSL, Marsee MA (2012) Exploring Narcissism, Psychopathy, and Machiavellianism in Youth: Examination of Associations with Antisocial Behavior and Aggression. Journal of Child and Family Studies:1-13.

Lynam DR, Derefinko KJ, Caspi A, Loeber R, Stouthamer-Loeber M (2007) The Content Validity of Juvenile Psychopathy: An Empirical Examination. Psychological Assessment 19 (3):363-367.

Malik AI, Zai CC, Abu Z, Nowrouzi B, Beitchman JH (2012) The role of oxytocin and oxytocin receptor gene variants in childhood-onset aggression. Genes, Brain and Behavior 11 (5):545-551.

Manuck SB, Flory JD, Ferrell RE, Mann JJ, Muldoon MF (2000) A regulatory polymorphism of the monoamine oxidase-A gene may be associated with variability in aggression, impulsivity, and central nervous system serotonergic responsivity. Psychiatry Research 95 (1):9-23.

Marsh AA, Finger EC, Fowler KA, Jurkowitz ITN, Schechter JC, Yu HH, Pine DS, Blair RJR (2011a) Reduced amygdala-orbitofrontal connectivity during moral judgments in youths with disruptive behavior disorders and psychopathic traits. Psychiatry Research - Neuroimaging 194 (3):279-286.

Marsh AA, Finger EC, Mitchell DGV, Reid ME, Sims C, Kosson DS, Towbin KE, Leibenluft E, Pine DS, Blair RJR (2008) Reduced amygdala response to fearful expressions in children

and adolescents with callous-unemotional traits and disruptive behavior disorders. American Journal of Psychiatry 165 (6):712-720.

Marsh AA, Finger EC, Schechter JC, Jurkowitz ITN, Reid ME, Blair RJR (2011b) Adolescents with psychopathic traits report reductions in physiological responses to fear. Journal of Child Psychology and Psychiatry and Allied Disciplines 52 (8):834-841.

Meyer-Lindenberg A, Buckholtz JW, Kolachana B, Hariri AR, Pezawas L, Blasi G, Wabnitz A, Honea R, Verchinski B, Callicott JH, Egan M, Mattay V, Weinberger DR (2006) Neural mechanisms of genetic risk for impulsivity and violence in humans. Proceedings of the National Academy of Sciences of the United States of America 103 (16):6269-6274.

Mitchell DGV (2011) The nexus between decision making and emotion regulation: A review of convergent neurocognitive substrates. Behavioural Brain Research 217 (1):215-231.

Munafò MR, Brown SM, Hariri AR (2008) Serotonin Transporter (5-HTTLPR) Genotype and Amygdala Activation: A Meta-Analysis. Biological Psychiatry 63 (9):852-857.

Muñoz LC, Qualter P, Padgett G (2011) Empathy and bullying: Exploring the influence of callous-unemotional traits. Child Psychiatry and Human Development 42 (2):183-196.

Odgers CL, Caspi A, Broadbent JM, Dickson N, Hancox RJ, Harrington H, Poulton R, Sears MR, Thomson WM, Moffitt TE (2007) Prediction of differential adult health burden by conduct problem subtypes in males. Archives of General Psychiatry 64 (4):476-484.

Pardini DA, Byrd AL (2012) Perceptions of aggressive conflicts and others' distress in children with callous-unemotional traits: 'I'll show you who's boss, even if you suffer and I get in trouble'. Journal of Child Psychology and Psychiatry and Allied Disciplines 53 (3):283-291.

Pardini DA, Fite PJ (2010) Symptoms of conduct disorder, oppositional defiant disorder, attention-deficit/hyperactivity disorder, and callous-unemotional traits as unique predictors of psychosocial maladjustment in boys: Advancing an evidence base for DSM-V. Journal of the American Academy of Child and Adolescent Psychiatry 49 (11):1134-1144.

Pardini DA, Lochman JE, Powell N (2007) The development of callous-unemotional traits and antisocial behavior in children: Are there shared and/or unique predictors? Journal of Clinical Child and Adolescent Psychology 36 (3):319-333.

Pasalich DS, Dadds MR, Hawes DJ, Brennan J (2011) Do callous-unemotional traits moderate the relative importance of parental coercion versus warmth in child conduct problems? An observational study. Journal of Child Psychology and Psychiatry 52 (12):1308-1315.

Passamonti L, Fairchild G, Goodyer IM, Hurford G, Hagan CC, Rowe JB, Calder AJ (2010) Neural abnormalities in early-onset and adolescence-onset conduct disorder. Archives of General Psychiatry 67 (7):729-738.

Rijsdijsk FV, Viding E, De Brito S, Forgiarini M, Mechelli A, Jones AP, McCrory E (2010) Heritable variations in gray matter concentration as a potential endophenotype for psychopathic traits. Archives of General Psychiatry 67 (4):406-413.

Rowe R, Costello EJ, Angold A, Copeland WE, Maughan B (2010) Developmental pathways in oppositional defiant disorder and conduct disorder. Journal of Abnormal Psychology 119 (4):726-738.

Rubia K (2011) "Cool" inferior frontostriatal dysfunction in attention-deficit/hyperactivity disorder versus "hot" ventromedial orbitofrontal-limbic dysfunction in conduct disorder: A review. Biological Psychiatry 69 (12): 69-87.

Rubia K, Smith AB, Halari R, Matsukura F, Mohammad M, Taylor E, Brammer MJ (2009) Disorder-specific dissociation of orbitofrontal dysfunction in boys with pure conduct disorder during reward and ventrolateral prefrontal dysfunction in boys with pure ADHD during sustained attention. American Journal of Psychiatry 166 (1):83-94.

Sadeh N, Javdani S, Jackson JJ, Reynolds EK, Potenza MN, Gelernter J, Lejuez CW, Verona E (2010) Serotonin transporter gene associations with psychopathic traits in youth vary as a function of socioeconomic resources. Journal of Abnormal Psychology 119 (3):604-609.

Sadeh N, Javdani S, Verona E (2012) Analysis of Monoaminergic Genes, Childhood Abuse, and Dimensions of Psychopathy. Journal of Abnormal Psychology. Advance online publication.

Scott S, Knapp M, Henderson J, Maughan B (2001) Financial cost of social exclusion: Follow up study of antisocial children into adulthood. BMJ 323 1–5

Schwenck C, Mergenthaler J, Keller K, Zech J, Salehi S, Taurines R, Romanos M, Schecklmann M, Schneider W, Warnke A, Freitag CM (2012) Empathy in children with autism and conduct disorder: Group-specific profiles and developmental aspects. Journal of Child Psychology and Psychiatry and Allied Disciplines 53 (6):651-659.

Sebastian CL, McCrory EJP, Cecil CAM, Lockwood PL, De Brito SA, Fontaine NMG, Viding E (2012) Neural responses to affective and cognitive theory of mind in children with conduct problems and varying levels of callous-unemotional traits. Archives of General Psychiatry 69 (8):814-822.

Shaw P, Gogtay N, Rapoport J (2010) Childhood psychiatric disorders as anomalies in neurodevelopmental trajectories. Human Brain Mapping 31 (6):917-925.

Sherer YC, Nickerson AB (2010) Anti-bullying practices in american schools: Perspectives of school psychologists. Psychology in the Schools 47 (3):217-229.

Smith PK, Pepler D, Rigby K (2004) Bullying in schools: How successful can interventions be? Cambridge University Press,

Sterzer P, Stadler C (2009) Neuroimaging of aggressive and violent behaviour in children and adolescents. Frontiers in Behavioral Neuroscience 3.

Sumich A, Sarkar S, Hermens DF, Kelesidi K, Taylor E, Rubia K (2012) Electrophysiological correlates of CU traits show abnormal regressive maturation in adolescents with conduct problems. Personality and Individual Differences 53 (7):862-867.

Sylvers PD, Brennan PA, Lilienfeld SO (2011) Psychopathic traits and preattentive threat processing in children: A novel test of the fearlessness hypothesis. Psychological Science 22 (10):1280-1287.

Taylor J, Loney BR, Bobadilla L, Iacono WG, McGue M (2003) Genetic and Environmental Influences on Psychopathy Trait Dimensions in a Community Sample of Male Twins. Journal of Abnormal Child Psychology 31 (6):633-645.

Viding E, Blair RJR, Moffitt TE, Plomin R (2005) Evidence for substantial genetic risk for psychopathy in 7-years-olds. Journal of Child Psychology and Psychiatry and Allied Disciplines 46 (6):592-597.

Viding E, Fontaine NMG, Oliver BR, Plomin R (2009) Negative parental discipline, conduct problems and callous-unemotional traits: Monozygotic twin differences study. British Journal of Psychiatry 195 (5):414-419.

Viding E, Frick PJ, Plomin R (2007) Aetiology of the relationship between callous-unemotional traits and conduct problems in childhood. British Journal of Psychiatry 49 33-38

Viding E, Hanscombe KB, Curtis CJC, Davis OSP, Meaburn EL, Plomin R (2010) In search of genes associated with risk for psychopathic tendencies in children: A two-stage genome-wide association study of pooled DNA. Journal of Child Psychology and Psychiatry and Allied Disciplines 51 (7):780-788.

Viding E, Jones AP (2008) Cognition to genes via the brain in the study of conduct disorder. Quarterly Journal of Experimental Psychology 61 (1):171-181.

Viding E, Jones AP, Frick PJ, Moffitt TE, Plomin R (2008) Heritability of antisocial behaviour at 9: Do callous-unemotional traits matter? Developmental Science 11 (1):17-22.

Viding E, McCrory EJ, Blakemore SJ, Frederickson N (2011) Behavioural problems and bullying at school: Can cognitive neuroscience shed new light on an old problem? Trends in Cognitive Sciences 15 (7):289-291.

Viding E, Sebastian CL, Dadds MR, Lockwood PL, Cecil CAM, De Brito SA, McCrory EJ (2012) Amygdala response to preattentive masked fear in children with conduct problems: The role of callous-unemotional traits. American Journal of Psychiatry 169 (10):1109-1116.

White SF, Marsh AA, Fowler KA, Schechter JC, Adalio C, Pope K, Sinclair S, Pine DS, Blair RJR (2012) Reduced amygdala response in youths with disruptive behavior disorders and psychopathic traits: Decreased emotional response versus increased top-down attention to nonemotional features. American Journal of Psychiatry 169 (7):750-758.

Yang Y, Raine A (2009) Prefrontal structural and functional brain imaging findings in antisocial, violent, and psychopathic individuals: A meta-analysis. Psychiatry Research - Neuroimaging 174 (2):81-88.