# The development of psychopathy

**R.J.R. Blair,[1] K.S. Peschardt,[1] S. Budhani,[1,2] D.G.V. Mitchell,[1] and D.S. Pine[1]**

[1]Mood and Anxiety Disorders Program, National Institute of Mental Health, National Institutes of Heath, Department of Health and Human Services, Bethesda, MD, USA; [2]Department of Psychology, University College London, UK

The current review focuses on the construct of psychopathy, conceptualized as a clinical entity that is fundamentally distinct from a heterogeneous collection of syndromes encompassed by the term 'conduct disorder'. We will provide an account of the development of psychopathy at multiple levels: ultimate causal (the genetic or social primary cause), molecular, neural, cognitive and behavioral. The following main claims will be made: (1) that there is a stronger genetic as opposed to social ultimate cause to this disorder. The types of social causes proposed (e.g., childhood sexual/physical abuse) should elevate emotional responsiveness, not lead to the specific form of reduced responsiveness seen in psychopathy; (2) The genetic influence leads to the emotional dysfunction that is the core of psychopathy; (3) The genetic influence at the molecular level remains unknown. However, it appears to impact the functional integrity of the amygdala and orbital/ventrolateral frontal cortex (and possibly additional systems); (4) Disruption within these two neural systems leads to impairment in the ability to form stimulus–reinforcement associations and to alter stimulus–response associations as a function of contingency change. These impairments disrupt the impact of standard socialization techniques and increase the risk for frustration-induced reactive aggression respectively.

The goal of the present paper is to provide as full an account of the development of psychopathy as possible. To explain a disorder, we need an account of the development of that disorder at multiple levels: ultimate causal (the genetic or social primary cause), molecular, neural, cognitive and behavioral. We need to be able to say how the genetic or social primary cause leads to specific receptor-level, molecular anomalies that impact on the functioning of specific neural systems such that specific cognitive functions are dysfunctional and a particular behavioral profile emerges. Of course, we have not reached that stage in understanding psychopathy. This paper will review what is currently known.

One major tenet to our argument is that psychopathy is a construct that is unique, relative to other syndromes captured in the current psychiatric nosology. The classification of psychopathy was introduced by Hare (1980, 1991). It is a developmental disorder in that it can be identified in both childhood and adulthood (Frick, O'Brien, Wootton, & McBurnett, 1994; Hare, 1980, 1991). Longitudinal studies showing that those identified as psychopathic in childhood are also identified as psychopathic in adulthood have not yet been done. However, the neuro-cognitive impairments seen in children with psychopathic tendencies are, for the most part, also seen in adults with psychopathic tendencies (see below).

The classification of psychopathy identifies a relatively homogeneous pathology (at least when compared with the diagnoses of conduct disorder [CD] and antisocial personality disorder [APD]). Unlike CD and APD, psychopathy involves a pervasive pattern of both emotional (considerably reduced empathy and guilt) and behavioral (criminal activity and, frequently, violence) symptoms (Frick et al., 1994; Hare, 1980, 1991). We argue that the emotional component is the crucial component of psychopathy. There are many developmental routes to an elevated risk for antisocial behavior (Blair, 2001; Silverthorn & Frick, 1999). The emotional dysfunction that is at the heart of psychopathy is only one such route. However, it is one that puts the individual at heightened risk for learning antisocial behaviors. Although, as will be argued, it does not *necessarily* mean that the individual *will* learn to be antisocial; whether he/she does or not will be determined by a constellation of individual and social factors.

The problem with the diagnoses of CD and APD is that because they focus on the behavioral feature of antisocial behavior, they do not differentiate between potential causes for its development. As a result, only approximately 25% of individuals classified with either of CD or APD will show psychopathic tendencies (Hart & Hare, 1996). Indeed, children with CD are a heterogeneous population. One child with CD might show the marked reduction in anxiety, empathy and guilt associated with psychopathy whilst another child with CD might show an opposite pathology – markedly elevated levels of anxiety. In contrast, we would like to believe that all appropriately identified individuals with psychopathy should share some feature of basic pathophysiology.

A core feature of the behavioral profile of children and adults with psychopathy is their excessive use of instrumental (a.k.a. proactive and planned) aggression (Cornell et al., 1996; Frick, Cornell, Barry, Bodin, & Dane, 2003). Instrumental aggression is purposeful and goal-directed aggression, used instrumentally to achieve a specific desired goal such as obtaining the victim's possessions (Berkowitz, 1993). In contrast, reactive (a.k.a. affective, impulsive, defensive) aggression is triggered by a

frustrating or threatening event and is often associated with anger (Barratt, Stanford, Dowdy, Liebman, & Kent, 1999; Berkowitz, 1993; Crick & Dodge, 1996). Elevated levels of reactive aggression are found in many disorders including psychopathy (see, for a review, Blair, 2003c). However, individuals with psychopathy show particularly elevated levels of instrumental aggression, relative to individuals with other syndromes associated with behavioral dyscontrol.

At the anatomical level, we have followed the work of Siegel and Panksepp suggesting that reactive aggression is mediated by a basic threat system that runs from medial amygdaloidal areas down to the dorsal half of the periaqueductal gray (e.g., Gregg & Siegel, 2001; Panksepp, 1998). We have suggested that this system is regulated by orbital, medial and ventrolateral frontal cortex (Blair, 2004; Grafman, Schwab, Warden, Pridgen, & Brown, 1996) and that it can become dysfunctional in two broad ways (Blair, 2004): First, the basic threat system may become elevated in its responsiveness due to endogenous (e.g., genetic) or exogenous (e.g., trauma; see below) factors. Second, the frontal systems regulating its activity may become dysfunctional. We will argue below that trauma can lead to increased responsiveness of the basic threat circuitry and therefore a greater risk for the individual expressing an extreme response (reactive aggression) to a mild threat rather than the more ecologically appropriate one (freezing or escape behavior). We will also argue below that the increased risk for reactive aggression seen in psychopathy is not to this type of dysfunction; the threat circuitry in psychopathy (at least the amygdala) is under-responsive rather than over-responsive. We will argue instead that the increased risk for reactive aggression in psychopathy is related to dysfunction in the regulatory activity of ventrolateral prefrontal cortex.

With respect to instrumental aggression, there have been suggestions that animal work on the neurobiology of predatory aggression may be informative regarding human instrumental aggression (Gregg & Siegel, 2001). However, animal predatory aggression is not displayed towards conspecifics while human instrumental aggression is almost always displayed towards conspecifics. Moreover, human instrumental aggression is goal directed and highly influenced by the individuals' learning history. Because instrumental aggression is a goal-directed motor response, we argue that it recruits the same neural regions as any other goal-directed activity; i.e., striatal and premotor cortical neurons (Passingham & Toni, 2001). We argue that the pathology leading to heightened levels of proactive aggression relates to socialization; because of impairment in specific forms of emotional learning, the child does not learn to avoid antisocial behavior.

As noted above, children and adults with psychopathy show heightened levels of both reactive and instrumental aggression. We will argue that the explanations of the increased risk for instrumental and reactive aggression seen in psychopathy may be independent at the neural and cognitive levels though we assume, once an adequate genetic/molecular account is available, that they are fundamentally related. In other words, there may be a single genetic contribution to two, or more, functionally relatively independent neuro-cognitive dysfunctions.

## Ultimate causes

By ultimate causes, we are referring to factors that are hypothesized to give rise to the basic pathology (the emotion dysfunction) that, we argue, is at the heart of the disorder. In this section, we are not considering factors (e.g., poor parenting, unemployment) that likely influence the behavioral manifestation of psychopathy but which, in our opinion, do not cause the primary emotion dysfunction seen in psychopathy. These influences will, however, be briefly discussed separately below. The ultimate causes we will consider are genes, physical/sexual abuse and brain damage (for example, from alcohol/drug abuse during pregnancy or birth complications).

### Psychopathy and genes

There has been a long behavioral genetic literature examining genetic influences on aggression and antisocial behavior more generally (Miles & Carey, 1997; Rhee & Waldman, 2002). This literature has provided heritability estimates for dimensional measures of aggression ranging from 44% to 72% in adults. However, this literature is difficult to interpret. First, because any genetic impact is likely to be complex and may be expressed as a function of an interaction with environmental factors (Caspi et al., 2002). Second, because this literature typically treats aggression as a unitary construct, there is no division between reactive and instrumental aggression. Third, because the literature has, on occasion, implied a genetic basis to individual antisocial behaviors. It is extremely unlikely that there is a direct genetic contribution to these specific *behaviors*, or at least it is as likely as there is a direct genetic contribution to an individual using an ATM machine to gain money. An individual learns to use an ATM and under particular conditions might also learn to become a pimp.

Genetic variation is likely to play a role is in determining the probability that the individual will *learn* an antisocial strategy to gain money (e.g., becoming a pimp) as opposed to a strategy sanctioned by society (using an ATM machine at the end of the workday). Many have argued that the emotional dysfunction shown by individuals with psychopathy makes them more likely to learn antisocial strategies to reach goals (Blair, 1995; Eysenck,

1964; Lykken, 1995; Trasler, 1973). These strategies fundamentally involve navigation of complex situations involving multiple emotionally salient cues. As such, this suggests that there may a genetic contribution to the emotional dysfunction *behind* the behavior, and that it is this association with emotional dysfunction which underlies the genetic contribution to antisocial behavior. Three recent studies provide support for this suggestion. In adults, Blonigen and colleagues (Blonigen, Carlson, Krueger, & Patrick, 2003) collected data from 353 male twins using the self-report Psychopathic Personality Inventory [PPI] (Lilienfeld & Andrews, 1996) and found moderate heritability ($h^2$ = .29 to .56) for the affect-based subscales of the measure (Blonigen et al., 2003). Blonigen and colleagues (2005) collected data from 626 pairs of 17-year-old male and female twins using the Multidimensional Personality Questionnaire and found significant heritability ($h^2$ = .46 to .51) for the two measures of psychopathic traits indexed [Fearless dominance and Impulsive Antisociality]; (Blonigen, Hicks, Krueger, Patrick, & Iacono, 2005). In children, examining almost 3,500 twin pairs within the Twins Early Development Study (TEDS), the callous and unemotional component of psychopathic tendencies was indexed at age 7 (Viding, Blair, Moffitt, & Plomin, 2005). This study revealed a significant group heritability of $h^2$ g = .67 and no shared environmental influence on the callous-unemotional component; i.e., genetic factors account for two-thirds of the difference between the callous-unemotional pro-bands and the population.

## A social basis to psychopathy?

There is considerable belief amongst the lay population, at least, that social factors, such as abuse, might cause psychopathy. Certainly, there is considerable evidence in humans of an association between physical and sexual abuse and increased risk of aggression and impulsivity (Dodge, Pettit, Bates, & Valente, 1995; Farrington & Loeber, 2000; Widom, 1992). Similarly, considerable data indicates that exposure to violence in the home/neighborhood increases the risk for aggression (e.g., Miller, Wasserman, Neugebauer, Gorman-Smith, & Kamboukos, 1999; Schwab-Stone et al., 1999). However, our position is that abuse/exposure to other extreme traumas potentiates specific neural systems involved in the individual's response to threat and by doing so increases the risk of reactive aggression and through this, increases the probability of a diagnosis of CD (see below). In contrast, we believe that abuse is unlikely to lead to the affective 'flattening' that is core feature of psychopathy (though see Carrey, Butter, Persinger, & Bialik, 1995).

Considerable work with animals has revealed the neurobiological impact of acute and prolonged threat/stress on aggressive behavior. Stimulation of the superior colliculus, a sub-cortical region involved in the mammalian basic response to threat (Gregg & Siegel, 2001; Panksepp, 1998), can potentiate the responsiveness of this system. This stimulation can increase levels of threat-relevant behavior for at least 3 months afterwards (King, 1999). In addition, the neuro-chemical response to threat can be profoundly affected throughout the lifespan by prior threat experience, particularly if this occurs early in life (Bremner & Vermetten, 2001; Charney, 2003).

The mammalian response to threat is gradated. At low levels of danger, from a distant threat, animals freeze. At higher levels, from a closer threat, they attempt to escape. At higher levels still, when the threat is very close and escape is impossible, the animal initiates reactive aggression (Blanchard, Blanchard, & Takahashi, 1977). In other words if, as appears to be the case (Bremner & Vermetten, 2001; Charney, 2003; King, 1999), prior threat exposure increases the individual's responsiveness to threat, then an individual who has been abused will be more likely to display reactive aggression to a lower-level threat than an individual who has not been so exposed. We believe that this is the origin of the association between child abuse and increased risk of aggression (Farrington & Loeber, 2000; Widom, 1992); lower-level threats, or more distal threats, can elicit reactive aggression more easily in abused individuals than in individuals not abused. However, we do not believe, on the basis of the available data, that physical/sexual abuse is a key factor in the genesis of psychopathy. A defining feature of psychopathy is the reduction, *not* elevation, in the individual's responsiveness to threat (Cleckley, 1976; Hare, 1970; Lykken, 1995; Patrick, 1994). Indeed, it is even possible that the neurobiological basis of psychopathy may protect the individual with psychopathic tendencies from developing mood and anxiety disorders such as depression, anxiety and post traumatic stress disorder. Thus, traumatic exposure, including exposure to violence in the home/neighborhood, increases the risk for mood and anxiety disorders in general, though not all exposed to trauma will go on to develop these disorders (Gorman-Smith & Tolan, 1998; Schwab-Stone et al., 1999). We argue that trauma increases the risk for CD/ASPD as a function of increased levels of purely reactive aggression. We hypothesize that individuals with psychopathy are protected from these risk factors. Studies examining the emotional and behavioral dimensions of psychopathy independently report that anxiety level is *inversely* associated with the emotional dimension but *positively* associated with the antisocial behavior dimension (Frick, Lilienfeld, Ellis, Loney, & Silverthorn, 1999; Patrick, 1994; Verona, Patrick, & Joiner, 2001). In short, increases in anxiety are associated with increases in antisocial behavior, particularly reactive aggression, but decreases in the emotional component of psychopathy. Similarly, depression appears to be inversely associated with psychopathy (Lovelace & Gannon, 1999).

### Environmental insult

Birth complications such as anoxia and pre-eclampsia can give rise to brain damage. Babies who suffer birth complications are more likely to develop conduct disorder (CD), delinquency, and commit violence in adulthood, particularly when other psychosocial risk factors are present (Hodgins, Kratzer, & McNeil, 2001, 2002; Pine, Shaffer, Schonfeld, & Davies, 1997; Piquero & Tibbetts, 1999; Raine, 2002a; Raine et al., 1994).

Minor physical anomalies (MPAs) are relatively minor physical abnormalities consisting of such features as low-seated ears, adherent ear lobes, and a furrowed tongue. MPAs have been associated with disorders of pregnancy and are thought to be a marker for fetal neural mal-development towards the end of the first three months of pregnancy. MPAs can be caused by environmental factors acting on the fetus such as anoxia, bleeding, and infection though they can also have a genetic basis (Guy, Majorski, Wallace, & Guy, 1983). MPAs, like obstetric complications, have also been linked to the development of CD, delinquency, and violence in adulthood, again particularly when other psychosocial risk factors are present (Brennan et al., 1997; Mednick & Kandel, 1988; Raine, 2002a). Unfortunately, the literature has not considered whether birth complications/MPAs are a risk factor for the emergence of psychopathy or syndromes linked to heightened levels of reactive aggression. Moreover, there has been little consideration of why birth complications or problems during pregnancy, as indicated by MPAs, should interact with psychosocial behavior. It has been suggested that 'the presence of a negative psychosocial factor is required to "trigger" the biological risk factor ...' (p. 426, Raine, 2002a). It is unclear, however, how a psychosocial factor could trigger the biological risk factor. Instrumental aggression is goal-directed behavior. It is difficult to imagine how a particular state of a biological risk would *inevitably* trigger a specific form of instrumental behavior, i.e., instrumental aggression. A similar argument can be made for reactive aggression. Reactive aggression is a response to threat or frustration. It will not occur in the absence of environmental input. But it is not that the environmental input triggers the system into a state such that reactive aggression will be regularly displayed. Rather it is that reactive aggression will not be displayed without some form of environmental stimulus (such as an imagined threat).

*Summary:* We argue that there is a genetic contribution to the emotion dysfunction component of psychopathy. This, in turn, puts the individual at greater risk for the development of the full syndrome. This does not suggest that the genetic contribution is the only determinant of how the pathology manifests; it is highly likely that other factors including social factors will have an influence. However, it does suggest that the genetic contribution may be a prerequisite for the development of the disorder whilst these other factors will influence the full presentation.

Physical and sexual abuse and other environmental traumas can elevate the responsiveness of the basic threat circuitry and increase the probability that an individual might show reactive aggression (Blair, 2004). However, an elevated responsiveness of the basic threat circuitry is not seen in individuals with psychopathy but rather reduced responsiveness. This is inconsistent with suggestions that psychopathy might be due to early environmental trauma.

Birth complications are risk factors for violent antisocial behavior, particularly if they occur when other psychosocial risk factors are present (Mednick & Kandel, 1988; Raine, 2002b). Unfortunately, to our knowledge, no studies have evaluated whether birth complications and MPAs are associated with an increased risk for instrumental or reactive aggression or both. An increased risk for instrumental aggression would suggest that birth complications and MPAs are associated with dysfunction in systems responsible for emotional learning. An increased risk for reactive aggression would suggest that birth complications and MPAs are associated with dysfunction in systems responsible for the regulation of the basic threat system. We believe it is far more likely that birth complications and MPAs are associated with dysfunction in systems responsible for the regulation of the basic threat system (and thus an increased risk for reactive aggression). Indeed, work with animals shows that perinatal distress does lead to hypofunction in systems responsible the regulation of the basic threat system (Brake, Sullivan, & Gratton, 2000). We believe, on the basis of the current evidence, that it is unlikely that birth complications are associated with an increased risk for the instrumental aggression seen in individuals with psychopathy.

## A molecular neuroscience account of psychopathy

Given the suggestion above of a genetic basis to the emotional disorder that is the basis of psychopathy it would be useful to be able to determine which genes give rise to what sorts of effects at the molecular level. However, we are some way off from a molecular neuroscience account of psychopathy.

Several suggestions have been made. For example, it has been suggested that there may be serotonergic abnormalities in individuals with psychopathy (Soderstrom, Blennow, Manhem, & Forsman, 2001; Soderstrom, Blennow, Sjodin, & Forsman, 2003). However, the samples in the Soderstrom et al. studies involve individuals under forensic pretrial evaluation, a non-typical sample of individuals with psychopathy. Studies with more typical samples find

the usual relationship between reduced serotonergic response and increased levels of aggression (Coccaro, 1996) but no relationship with the emotional basis of psychopathy (Dolan & Anderson, 2003). We have argued elsewhere that the norepinephrine system may be implicated in the pathology of psychopathy (Blair, 2003b). Norepinephrine (NE) has a considerable role in the innervation of the neural systems involved in the basic response to threat in both animals and humans (Ferry, Roozendaal, & McGaugh, 1999; MacDonald & Scheinin, 1995). There have been provocative suggestions that NE is involved in mediating the impact of aversive cues in human choice (Rogers, Lancaster, Wakeley, & Bhagwager, submitted), and NE manipulations appear to selectively impact the processing of sad expressions (Harmer, Perrett, Cowen, & Goodwin, 2001). In addition, there have been a series of reports that high levels of antisocial behavior/conduct disorder are associated with reduced norepinephrine levels (Raine, 1993; Rogeness, Cepeda, Macedo, Fischer, & Harris, 1990). However, as yet the data with respect to psychopathy remains sparse and inconclusive.

*Summary:* While we believe that there is a genetic contribution to the emotion dysfunction component of psychopathy, how this contribution manifests itself at the molecular level is currently unknown.

## Neural systems implicated in psychopathy

While it remains unknown how the genetic contribution to psychopathy manifests at the molecular level, it appears clear that at the neural system level it manifests in at least two main systems: the amygdala and orbital/ventrolateral frontal cortex. These will each be briefly considered in turn. As a fundamental tenet to both considerations, we view these systems as neural circuits possessing precise functions in terms of information processing. Thus, delineation of information-processing deficits in a syndrome is a fundamental prerequisite to identifying circuitry involvement in complex syndromes, such as psychopathy. Moreover, given our view of psychopathy as a neurodevelopmental disorder, delineating normal functions of these circuits, both in developing and mature organisms, is fundamental to linking circuitry-based dysfunction to information processing deficits and their associated clinical manifestations.

### The amygdala and psychopathy

There are considerable indications of amygdala dysfunction in individuals with psychopathy (Blair, 2003b). Functional imaging studies have shown that adults with the disorder present with reduced amygdala activation during emotional memory (Kiehl et al., 2001) and aversive conditioning tasks (Birbaumer et al., 2005; Veit et al., 2002); though see (Muller et al., 2003). In addition, individuals with psychopathy present with impairment on a series of tasks which require the functional integrity of the amygdala. Thus, lesions of the amygdala disrupt aversive conditioning (Bechara et al., 1995; LaBar, LeDoux, Spencer, & Phelps, 1995), the augmentation of the startle reflex by visual threat primes (Angrilli et al., 1996), passive avoidance learning (Ambrogi Lorenzini, Baldi, Bucherelli, Sacchetti, & Tassoni, 1999) and fearful expression recognition (Adolphs, 2002; Blair, 2003a). Individuals with psychopathy show impairment in aversive conditioning (Flor, Birbaumer, Hermann, Ziegler, & Patrick, 2002), the augmentation of the startle reflex by visual threat primes (Levenston, Patrick, Bradley, & Lang, 2000), passive avoidance learning (Newman & Kosson, 1986) and fearful expression recognition (Blair, Colledge, Murray, & Mitchell, 2001). The functional impact of this amygdala dysfunction with respect to empathy, socialization and the development of instrumental aggression will be discussed further below.

### Frontal lobe dysfunction and psychopathy

Frontal lobe/executive function dysfunction has long been related to antisocial behavior with claims that either psychopathy in particular or antisocial behavior more generally is due to frontal lobe dysfunction (Gorenstein, 1982; Moffitt, 1993; Raine, 2002a). Three main strands of data support this contention: (1) individuals with antisocial behavior show impaired performance on classic measures of executive functioning (see, for reviews of this literature, Kandel & Freed, 1989; Morgan & Lilienfield, 2000); (2) neuro-imaging data indicate that aggressive individuals are marked by reduced frontal functioning (Goyer et al., 1994; Raine et al., 1998; Volkow et al., 1995); and (3) patients with lesions of frontal cortex, whether these occur early in life or adulthood, present with a heightened risk for aggression (Anderson, Bechara, Damasio, Tranel, & Damasio, 1999; Grafman et al., 1996; Pennington & Bennetto, 1993).

We have argued elsewhere that the frontal lobe positions need greater specification (Blair, 2004). Frontal cortex corresponds to almost half of the cortex (Fuster, 1980) and has been implicated in a wide variety of putative processes (Baddeley & Della Sala, 1998; Luria, 1966; Shallice & Burgess, 1996). However, the frontal lobe positions rarely specify which regions/executive processes are thought to be dysfunctional. Moreover, the frontal lobe dysfunction positions also have not specified whether they apply to reactive or instrumental aggression or both.

Fortunately, the existent data allow some specification of the frontal lobe dysfunction positions. The neurological literature indicates that only lesions of

orbital and ventrolateral frontal cortex, and not dorsolateral prefrontal cortex, are associated with increased risk of aggression (Grafman et al., 1996). Moreover, only the risk for reactive, and not instrumental, aggression is associated with such lesions (Anderson et al., 1999; Grafman et al., 1996; Pennington & Bennetto, 1993). Orbital and ventrolateral frontal cortex regulate the neural systems (the amygdala, hypothalamus and peri-aqueductal gray) that mediate the basic response to threat (including reactive aggression) (Gregg & Siegel, 2001; Panksepp, 1998). When they are dysfunctional the basic threat response becomes dys-regulated, increasing the risk for reactive aggression. Psychopathy is associated with an increased risk for both reactive and instrumental aggression (Cornell et al., 1996; Frick et al., 2003; Williamson et al., 1987).

In other words, a frontal lobe dysfunction position, even if specified in detail, is unlikely to be able to account for the development of the full syndrome. However, there are indications of orbital/ventrolateral frontal cortex dysfunction in individuals with psychopathy. Animal and human lesion studies, as well as recent functional imaging studies, all strongly indicate a role of orbital/ventrolateral frontal cortex in response reversal and extinction (Cools, Clark, Owen, & Robbins, 2002; Rolls, 1997; Rolls, Hornak, Wade, & McGrath, 1994); see also below. Individuals with psychopathy show marked problems in response reversal/extinction (LaPierre, Braun, & Hodgins, 1995; Mitchell, Colledge, Leonard, & Blair, 2002; Newman, Patterson, & Kosson, 1987).

### Dysfunction beyond the amygdala and orbital/ventrolateral frontal cortex

It is unlikely that the genetic contribution to psychopathy only affects the amygdala and orbital/ventrolateral frontal cortex. However, it is currently unknown whether the genetic contribution influences regions beyond these systems. On the basis of neuro-imaging data, Kiehl (in press) has argued that there is dysfunction in individuals with psychopathy within paralimbic cortex (i.e., amygdala, anterior superior temporal gyrus, rostral and caudal anterior cingulate, posterior cingulate, ventromedial frontal cortex and parahippocampal regions). However, neuro-imaging data is notoriously unable to localize deficits; impairment in any region will lead to anomalous activity in any region reliant on the dysfunctional region for input. We can only be sure that an area is dysfunctional in a population if both neuro-imaging and neuropsychological data indicate impairment. Indeed, anterior cingulate, at least, does not appear globally impaired in individuals with psychopathy. Damage to anterior cingulate is known to increase the Stroop effect; i.e., the interference by distracter information (Stuss, Gallup, & Alexander, 2001). However, individuals with psychopathy show

no evidence of increases in the Stroop effect, if anything the opposite (Hiatt, Schmitt, & Newman, 2004; Peschardt et al., in press b).

*Summary:* Earlier positions suggesting that frontal lobe dysfunction is a risk factor for antisocial behavior more generally or psychopathy in particular required specification. This has occurred. Orbital and ventrolateral dysfunction is a risk factor specifically for reactive aggression; in the healthy individual these regions are involved in regulating the neural systems that mediate the basic response to threat (which, at its most extreme, is reactive aggression). These regions appear dysfunctional in psychopathy and, we believe, put individuals with this disorder at heightened risk for inappropriate displays of reactive aggression. In addition, we believe that psychopathy is marked by amygdala dysfunction. We believe this dysfunction disrupts the ability of the individual to be socialized and thus puts them at greater risk of learning antisocial behaviors, including instrumental aggression, to achieve their goals (see below).

## Cognitive dysfunction in psychopathy

The use of the term cognitive here refers to a functional capacity of a given neural system/neural circuit whether the circuitry involved includes 'limbic' structures or not. Thus, for example, our neural account of psychopathy above suggested amygdala dysfunction and the comparable cognitive account to be described will suggest impairment in stimulus–reinforcement association formation.

### 'Executive' accounts of psychopathy

We term Lynam's impulse control and Newman's response set modulation models executive accounts because they suggest the existence of general systems operating on multiple domains. These accounts do not deny the existence of emotional deficits in psychopathic individuals. However, they suggest that these emotional deficits are secondary to putative executive deficits.

Executive dysfunction in psychopathy has been linked to impulsivity (Miller, Flory, Lynam, & Leukefeld, 2003; Whiteside & Lynam, 2001), conceptualized as (lack of) premeditation and (lack of) perseverance, where lack of premeditation is likened to the 'inability to inhibit previously rewarded behavior when presented with changing contingencies' (Whiteside & Lynam, 2001) and lack of perseverance 'may be related to disorders that involve the inability to ignore distracting stimuli or to remain focused on a particular task' (Whiteside & Lynam, 2001). In addition, executive dysfunction in psychopathy has been linked to impaired response set modulation – the 'rapid and relatively automatic (i.e., non-effortful or involuntary) shift of attention from

the effortful organization and implementation of goal-directed behavior to its evaluation' (Patterson & Newman, 1993; Newman, 1998).

From these accounts it could be expected that individuals with psychopathy would be impaired on a broad range of tasks; many tasks can be considered to involve inhibition or response set modulation (e.g., the intra-dimensional/extra-dimensional (ID/ED) and spatial alteration/object alteration tasks). In these tasks, there are two principal measures: First, the number of response reversal errors/object reversals. Second, the number of ED errors/spatial reversals (e.g., in the ID/ED task, when the participant responds by choosing one or other shape despite the fact that the reward contingency is based on the lines which accompany the shapes). Response/object reversal, ED shifting and spatial alteration would all appear to require the inhibition of a previously rewarded behavior/response modulation. However, while inhibition or response modulation accounts can explain the response/object reversal impairment shown by individuals with psychopathy, they have more difficulty explaining the lack of an impairment in ED shifting/spatial alteration shown by the same individuals (Mitchell et al., 2002; Peschardt et al., in press b). Yet an account of these data can be provided from the perspective of cognitive neuroscience. Thus, as we argued above, individuals with psychopathy are impaired in those processes, mediated by orbital/ventrolateral frontal cortex, that allow the alternation of responding to different *objects* as a function of contingency change. However, they are unimpaired in those processes, mediated by dorsolateral prefrontal cortex, that allow the alternation of responding to different conceptual *categories* (shapes vs. lines) or spatial locations as a function of contingency change. In short, even if a characterization of the impairment in individuals with psychopathy in terms of inhibition or response modulation was correct, we argue that it would be necessary to constrain such accounts such that they were not domain general but rather specific to particular neuro-cognitive systems.

### Stimulus–reinforcement associations, fear, empathy, moral socialization and instrumental antisocial behavior

The amygdala is necessary for the formation of stimulus–reinforcement associations (Baxter & Murray, 2002; Everitt, Cardinal, Parkinson, & Robbins, 2003) and, it is claimed, individuals with psychopathy are impaired in the formation of stimulus–reinforcement associations (Blair, 2004). Impairment in the formation of aversive stimulus–reinforcement associations would give rise to the observed deficits in individuals with psychopathy in aversive conditioning (Lykken, 1957), the augmentation of the startle reflex following the presentation

of visual threat primes (Levenston et al., 2000) and passive avoidance learning (Newman & Kosson, 1986). In short, impairment in the formation of aversive stimulus–reinforcement associations would give rise to the deficits consistent with previous suggestions (Lykken, 1957; Patrick, 1994) that there is fear system dysfunction in psychopathy (Blair, 2004).

One class of aversive stimuli is the distress of other individuals, the expressions of fear and sadness (Blair, 2003a). The amygdala is involved in the response to these stimuli (Blair, 2003a; Morris et al., 1996). In line with suggestions of a specific form of empathy deficit, individuals with psychopathy show reduced autonomic responses to the distress cues of other individuals and impaired fearful facial and vocal expression recognition (see, for a review, Blair, 2003a).

The argument has been made that the expressions of fear and sadness serve as social reinforcers allowing conspecifics to teach the societal valence of objects and actions to the developing individual (Blair, 2003a); actions/objects associated with the sadness/fear of others acquire, in healthy developing children, negative valence. Due to their impairment in the response to the sadness and fear of other individuals and in the formation of aversive stimulus–reinforcement associations, individuals with psychopathy are less able to take advantage of this 'moral' social referencing. They should be, and are (Oxford, Cavell, & Hughes, 2003; Wootton, Frick, Shelton, & Silverthorn, 1997), more difficult to socialize through standard parenting techniques. They will not learn to avoid using instrumental antisocial behavior to achieve their goals. This is because of relative indifference to the 'punishment' of the victim's distress and impairment in learning the association between this 'punishment' and the representation of the action that caused the victim's distress. If confirmed, this observation should have fundamental implications for treatment. The nature of interventions directed to children with severe conduct problems should vary based on the degree to which the specific child exhibits the emotional features of psychopathy.

The amygdala is known to be involved in not only the processing of punishment but also reward information (Baxter & Murray, 2002; Everitt et al., 2003). Individuals with psychopathy typically show appropriate suppression of the startle reflex following the presentation of positive visual primes but reduced augmentation of the startle reflex following the presentation of negative visual primes (Levenston et al., 2000; Patrick, Bradley, & Lang, 1993), though see (Herpertz et al., 2001). This suggests that individuals with psychopathy are unimpaired in processing positive material. However, in lexical decision-making tasks where participants must identify words versus non-words, comparison individuals are faster to identify positive and negative

emotional words than neutral ones, but individuals with psychopathy do not show this emotional advantage (Lorenz & Newman, 2002; Williamson et al., 1991). In addition, Verona and colleagues reported reduced skin conductance responses to both positive and negative auditory stimuli in individuals with psychopathy (Verona, Curtin, Patrick, Bradley, & Lang, 2004). Finally, in recent work within our own group, using affective priming (Peschardt, Morton, & Blair, under revision), decision-making (Peschardt et al., in press a) and emotional attention paradigms (Mitchell, Richell, Leonard, & Blair, in press), we have found impaired processing of both positive and negative material, but that this impairment is particularly severe for negative material.

Our assumption is that appetitive stimulus–reinforcement association formation is impaired, but less impaired than aversive stimulus–reinforcement association formation (Blair, 2004). Interestingly, given this claim that stimulus–reward association formation is less impaired in individuals with psychopathy than stimulus–punishment association formation, Kochanska has reported data indicating that conscience development in 'fearless' children is best achieved by socialization practices that presumably capitalize on mother–child positive orientation (secure attachment, maternal responsiveness); (Kochanska, 1997).

Interestingly, the amygdala is not involved in all forms of reinforcement-based learning. For example, it is not involved in stimulus–response association formation (Baxter & Murray, 2002). Some instrumental learning tasks cannot be solved through stimulus–reinforcement association formation and must be solved through the formation of stimulus–response associations; e.g., object discrimination. Object discrimination learning involves learning to respond to one of two objects (one rewarded and one not rewarded) repeatedly presented in a pair-wise fashion over a series of trials. In object discrimination tasks, the participant cannot learn that some of the stimuli are 'good' or 'bad' and should therefore be approached or avoided. This is because the compound stimulus (A plus B) can be both 'good' and 'bad'. Whether it is 'good' or 'bad' is determined by the response made to the stimulus. In line with this, individuals with psychopathy show no difficulty on object discrimination learning tasks (Budhani & Blair, in press; Budhani, Sullivan, & Gratton, in press; Mitchell et al., 2002).

### Altering stimulus–response associations as a function of contingency change, frustration and reactive aggression

The suggestion has been made that ventro-medial regions code expectancy of reinforcement and identify reinforcement contingency changes while ventro-lateral regions gate response choice following a detected change in reinforcement contingency (Blair, 2004). In short, damage to these regions will profoundly impair the individual's ability to alter stimulus–response associations, and corresponding behavior, to achieve expected rewards following a change in reinforcement contingency (i.e., a change such that an action that used to be rewarding now leads to punishment). Two tasks index the individual's ability to alter stimulus–response associations as a function of contingency change; response reversal and extinction. Individuals with psychopathy show impaired response reversal and extinction (LaPierre et al., 1995; Mitchell et al., 2002; Newman et al., 1987). This appears to be related to a reduced sensitivity to temporal difference errors; the difference between the expected reward and received reward (O'Doherty, Dayan, Friston, Critchley, & Dolan, 2003). The impairment shown by individuals with psychopathy becomes more marked, the more subtle the temporal difference error to be detected (Budhani & Blair, in press).

Frustration has long been linked to the display of reactive aggression (Berkowitz, 1993). Frustration occurs following the initiation of a behavior to achieve an expected reward and the subsequent absence of this reward. Impairment in the ability to alter stimulus–response associations as a function of contingency change means that the individual with psychopathy will be less able to flexibly alter their behavior in response to changes in the environment. In short, the individual will be at heightened risk for frustration-based reactive aggression.

*Summary:* At the cognitive level, the claim is that psychopathy is marked by two main forms of impairment: dysfunction in the ability to form stimulus–reinforcement associations and impairment in altering stimulus–response associations as a function of contingency change. Dysfunction in the ability to form stimulus–reinforcement associations is linked to the specific forms of 'fear' and 'empathy' deficits seen in psychopathy. This dysfunction is thought to disrupt the child's ability to be socialized and therefore put the child at risk for learning to use antisocial behavior to achieve their goals. Dysfunction in the ability to alter stimulus–response associations as a function of contingency change is a risk factor for frustration and consequent reactive aggression.

### Additional influences on the behavioral manifestation: the impact of social and environmental variables

We have argued here that there is a genetic contribution to the developmental integrity of the amygdala and orbital/ventrolateral frontal cortex (i.e., the emotional dysfunction that is the core of psychopathy), and that this leads to impairment in the ability to form stimulus–reinforcement associations

and to alter stimulus–response associations as a function of contingency change. These impairments interfere with the child's socialization and also increase the risk that he/she will show frustration-induced reactive aggression. This does not imply though that social/environmental factors play no role in the development of psychopathy. While the current literature has so far provided no evidence that any social/environmental factor leads to reduced amygdala functioning (and consequent reduced ability to form stimulus–reinforcement associations), there is considerable reason to believe that social/environmental variables influence the behavioral manifestation of psychopathy.

There are a variety of factors that are associated with an increased risk for antisocial behavior and aggression; for example, parenting variables including inconsistent parenting, an antisocial cultural and economic background and unemployment. Some of these variables probably have less influence on the behavior of individuals with psychopathy than healthy individuals because of the nature of the pathology. As noted above, for example, while poor parenting is a risk factor for increased conduct problems in healthy children, this is less the case for children who show the emotional dysfunction associated with psychopathy (Oxford et al., 2003; Wootton et al., 1997). As argued above, good parenting, including the use of empathy induction techniques, should increase aversion to antisocial behaviors (the person will associate the 'punishment' of the victim's distress with the antisocial behavior). Due to the dysfunction in stimulus–reinforcement association formation, individuals with psychopathic tendencies are far less able to take advantage of good parenting techniques. However, some of the variables may even have more impact on the probability of instrumental antisocial behavior in children with the emotion dysfunction that is the core of psychopathy. Children with psychopathic tendencies are at heightened risk for learning to use antisocial behaviors to achieve their goals. However, whether antisocial strategies are learnt and certainly whether they are implemented is likely to be highly dependent on their social circumstances. Family wealth/personal employment is going to determine whether the child has sufficient funds to achieve their goals in a socially typical fashion. Exposure to role models in either the family or on television is going to determine their level of exposure to potential antisocial strategies. The level of antisocial behavior shown by children with the emotion dysfunction that, we argue, is the core of psychopathy might even be under greater influence of these social variables. While the impact of these variables on the healthy child will be moderated by their empathic responsiveness, this will not be the case in the child with psychopathic tendencies.

*Summary:* Currently, to our knowledge, there are no data indicating any social/environmental factor leads to amygdala dysfunction and the specific form of reduced emotional responding seen in psychopathy. Moreover, some social environmental variables that have an impact on aggression/antisocial behaviors in typically developing children, such as abuse, exposure to violence in the environment and parenting techniques, are likely to have less of an impact on the behavior of children with the emotion dysfunction that is at the core of psychopathy. This is because, we argue, they have their impact through neuro-cognitive mechanisms that are dysfunctional in psychopathy; i.e., their impact cannot be expressed. However, other social environmental variables that have an impact on aggression/antisocial behaviors in typically developing children, for example, an antisocial cultural and economic background and unemployment, are likely to have at least as great an impact on the behavior of children with the emotion dysfunction that is at the core of psychopathy. This is because they influence either the motivation to offend or the child's knowledge base of antisocial strategies, neither of which is likely to be impaired in children with psychopathic tendencies.

## General conclusion

As noted above, to explain a disorder we need an account of the development of that disorder at the ultimate causal (genetic/social), molecular, neural, cognitive and behavioral levels. Fortunately, the classification of psychopathy, unlike the diagnoses of conduct disorder or antisocial personality disorder, identifies a relatively homogeneous population. There is a unitary disorder upon which a causal account can be developed.

On the basis of the current data, we believe that there is a genetic and not a social ultimate cause to this disorder. The types of social causes proposed (e.g., childhood sexual/physical abuse) should elevate emotional responsiveness, not lead to the specific form of reduced responsiveness seen in psychopathy. We believe that the genetic contribution is to the emotional dysfunction that is the core of psychopathy. While the impact of this contribution is not yet understood at the molecular level, we believe that neural systems that are disrupted include the amygdala and orbital/ventrolateral frontal cortex. At the cognitive level, disruption within these two crucial systems is mirrored by impairment in the ability to form stimulus–reinforcement associations and to alter stimulus–response associations as a function of contingency change.

Although this was not articulated above, we believe that it is at the cognitive level that the influence of social variables emerges. The ability to form stimulus–reinforcement associations is linked to the 'empathy' deficits seen in psychopathy and is thought to disrupt the child's ability to be socialized. The child is at heightened risk for learning to use antisocial behaviors to achieve their goals. However,

whether antisocial strategies are learnt is likely to be highly dependent on their social circumstances: for example, whether they have sufficient funds to achieve their goals in a socially typical fashion and therefore do not have to learn antisocial strategies. Dysfunction in the ability to alter stimulus–response associations following contingency change is a risk factor for frustration and consequent reactive aggression. However, the individual's environment will determine the frequency of contingency change; if it is rare, the individual should less frequently express frustration-induced reactive aggression.

In conclusion, we believe that considerable progress has been made in understanding the development of psychopathy. The work of Robert Hare has been crucial in identifying a relatively homogeneous population that can be the focus of scientific concern. This has allowed specification of the dysfunctional bases of the disorder, particularly at the neural and cognitive levels. What remains in its infancy, however, is an understanding of psychopathy at the genetic and molecular levels. However, such an understanding is at present being actively pursued.

## Acknowledgements

## Correspondence to

James Blair, Unit on Affective Cognitive Neuroscience, Mood and Anxiety Disorders Program, National Institute of Mental Health, 15K North Drive, Room 206, MSC 2670, Bethesda, Maryland 20892-2670, USA; Email: blairj@intra.nimh.nih.gov

## References

Adolphs, R. (2002). Neural systems for recognizing emotion. *Current Opinion in Neurobiology, 12,* 169–177.

Ambrogi Lorenzini, C.G., Baldi, E., Bucherelli, C., Sacchetti, B., & Tassoni, G. (1999). Neural topography and chronology of memory consolidation: A review of functional inactivation findings. *Neurobiology of Learning and Memory, 71,* 1–18.

Anderson, S.W., Bechara, A., Damasio, H., Tranel, D., & Damasio, A.R. (1999). Impairment of social and moral behaviour related to early damage in human prefrontal cortex. *Nature Neuroscience, 2,* 1032–1037.

Angrilli, A., Mauri, A., Palomba, D., Flor, H., Birhaumer, N., Sartori, G., et al. (1996). Startle reflex and emotion modulation impairment after a right amygdala lesion. *Brain, 119,* 1991–2000.

Baddeley, A., & Della Sala, S. (1998). Working memory and executive control. In A.C. Roberts, T.W. Robbins, & L. Weiskrantz (Eds.), *The prefrontal cortex* (pp. 9–21). New York: Oxford University Press.

Barratt, E.S., Stanford, M.S., Dowdy, L., Liebman, M.J., & Kent, T.A. (1999). Impulsive and premeditated aggression: A factor analysis of self-reported acts. *Psychiatry Research, 86,* 163–73.

Baxter, M.G., & Murray, E.A. (2002). The amygdala and reward. Nature Reviews. *Neuroscience, 3,* 563–73.

Bechara, A., Tranel, D., Damasio, H., Adolphs, R., Rockland, C., & Damasio, A.R. (1995). Double dissociation of conditioning and declarative knowledge relative to the amygdale and hippocampus in humans. *Science, 269,* 1115–1118.

Berkowitz, L. (1993). *Aggression: Its causes, consequences, and control.* Philadelphia: Temple University Press.

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

Blair, R.J.R. (1995). A cognitive developmental approach to morality: Investigating the psychopath. *Cognition, 57,* 1–29.

Blair, R.J.R. (2001). Neuro-cognitive models of aggression, the antisocial personality disorders and psychopathy. *Journal of Neurology, Neurosurgery and Psychiatry, 71,* 727–731.

Blair, R.J.R. (2003a). Facial expressions, their communicatory functions and neuro-cognitive substrates. Philosophical Transactions of the Royal Society London B. *Biological Science, 358,* 561–72.

Blair, R.J.R. (2003b). Neurobiological basis of psychopathy. *British Journal of Psychiatry, 182,* 5–7.

Blair, R.J.R. (2003c). A neuro-cognitive model of the psychopathic individual. In M.A. Ron & T.W. Robbins (Eds.), *Disorders of brain and mind 2* (pp. 400–420). Cambridge: Cambridge University Press.

Blair, R.J.R. (2004). The roles of orbital frontal cortex in the modulation of antisocial behavior. *Brain and Cognition, 55,* 198–208.

Blair, R.J.R., Colledge, E., Murray, L., & Mitchell, D.G. (2001). A selective impairment in the processing of sad and fearful expressions in children with psychopathic tendencies. *Journal of Abnormal Child Psychology, 29,* 491–498.

Blanchard, R.J., Blanchard, D.C., & Takahashi, L.K. (1977). Attack and defensive behaviour in the albino rat. *Animal Behavior, 25,* 197–224.

Blonigen, D.M., Carlson, S.R., Krueger, R.F., & Patrick, C.J. (2003). A twin study of self-reported psychopathic personality traits. *Personality and Individual Differences, 35,* 179–197.

Blonigen, D.M., Hicks, B.M., Krueger, R.F., Patrick, C.J., & Iacono, W.G. (2005). Psychopathic personality traits: Heritability and genetic overlap with internalizing and externalizing psychopathology. *Psychological Medicine, 35,* 637–648.

Brake, W.G., Sullivan, R.M., & Gratton, A. (2000). Perinatal distress leads to lateralized medial prefrontal cortical dopamine hypofunction in adult rats. *Journal of Neuroscience, 20,* 5538–5543.

Bremner, J.D., & Vermetten, E. (2001). Stress and development: Behavioral and biological conse-

quences. *Development and Psychopathology, 13,* 473–489.

Brennan, P.A., Raine, A., Schulsinger, F., Kirkegaard-Sorensen, L., Knop, J., Hutchings, B., et al. (1997). Psychophysiological protective factors for male subjects at high risk for criminal behavior. *American Journal of Psychiatry, 154,* 853–855.

Budhani, S., & Blair, R.J.R. (in press). Probabilistic response reversal in children with psychopathic tendencies. *Journal of Child Psychology and Psychiatry.*

Budhani, S., Richell, R.A., & Blair, R.J.R. (in press). Impaired reversal but intact acquisition: Probabilistic response reversal deficits in adult individuals with psychopathy. *Journal of Abnormal Psychology.*

Carrey, N.J., Butter, H.J., Persinger, M.A., & Bialik, R.J. (1995). Physiological and cognitive correlates of child abuse. *Journal of the American Academy of Child and Adolescent Psychiatry, 34,* 1067–1075.

Caspi, A., McClay, J., Moffitt, T.E., Mill, J., Martin, J., Craig, I.W., et al. (2002). Role of genotype in the cycle of violence in maltreated children. *Science, 297,* 851–854.

Charney, D.S. (2003). Neuroanatomical circuits modulating fear and anxiety behaviors. *Acta Psychiatrica Scandinavica Supplements,* 38–50.

Cleckley, H.M. (1976). *The mask of sanity.* St Louis, MO: Mosby.

Coccaro E.F. (1996). Neurotransmitter correlates of impulsive aggression in humans. *Annual New York Academy of Sciences, 794,* 82–89.

Cools, R., Clark, L., Owen, A.M., & Robbins, T.W. (2002). Defining the neural mechanisms of probabilistic reversal learning using event-related functional magnetic resonance imaging. *Journal of Neuroscience, 22,* 4563–4567.

Cornell, D.G., Warren, J., Hawk, G., Stafford, E., Oram, G., & Pine, D. (1996). Psychopathy in instrumental and reactive violent offenders. *Journal of Consulting and Clinical Psychology, 64,* 783–790.

Crick, N.R., & Dodge, K.A. (1996). Social information-processing mechanisms on reactive and proactive aggression. *Child Development, 67,* 993–1002.

Dodge, K.A., Pettit, G.S., Bates, J.E., & Valente, E. (1995). Social information-processing patterns partially mediate the effect of early physical abuse on later conduct problems. *Journal of Abnormal Psychology, 104,* 632–643.

Dolan, M.C., & Anderson, I.M. (2003). The relationship between serotonergic function and the Psychopathy Checklist: Screening version. *Journal of Psychopharmacology, 17,* 216–222.

Everitt, B.J., Cardinal, R.N., Parkinson, J.A., & Robbins, T.W. (2003). Appetitive behavior: Impact of amygdala-dependent mechanisms of emotional learning. *Annual New York Academy of Sciences, 985,* 233–250.

Eysenck, H.J. (1964). *Crime and personality.* London: Routledge & Kegan Paul.

Farrington, D.P., & Loeber, R. (2000). Epidemiology of juvenile violence. *Child and Adolescent Psychiatry Clinics of North America, 9,* 733–748.

Ferry, B., Roozendaal, B., & McGaugh, J.L. (1999). Involvement of alpha1-adrenoceptors in the basolateral amygdala in modulation of memory storage. *European Journal of Pharmacology, 372,* 9–16.

Flor, H., Birbaumer, N., Hermann, C., Ziegler, S., & Patrick, C.J. (2002). Aversive Pavlovian conditioning in psychopaths: Peripheral and central correlates. *Psychophysiology, 39,* 505–518.

Frick, P.J., Cornell, A.H., Barry, C.T., Bodin, S.D., & Dane, H.E. (2003). Callous-unemotional traits and conduct problems in the prediction of conduct problem severity, aggression, and self-report delinquency. *Journal of Abnormal Child Psychology, 31,* 457–70.

Frick, P.J., Lilienfeld, S.O., Ellis, M., Loney, B., & Silverthorn, P. (1999). The association between anxiety and psychopathy dimensions in children. *Journal of Abnormal Child Psychology, 27,* 383–392.

Frick, P.J., O'Brien, B.S., Wootton, J.M., & McBurnett, K. (1994). Psychopathy and conduct problems in children. *Journal of Abnormal Psychology, 103,* 700–707.

Fuster, J.M. (1980). *The prefrontal cortex.* New York: Raven Press.

Gorenstein, E.E. (1982). Frontal lobe functions in psychopaths. *Journal of Abnormal Psychology, 91,* 368–379.

Gorman-Smith, D., & Tolan, P. (1998). The role of exposure to community violence and developmental problems among inner-city youth. *Development and Psychopathology, 10,* 101–116.

Goyer, P.F., Andreason, P.J., Semple, W.E., Clayton, A.H., King, A.C., Compton-Toth, B.A., et al. (1994). Positron-emission tomography and personality disorders. *Neuropsychopharmacology, 10,* 21–28.

Grafman, J., Schwab, K., Warden, D., Pridgen, B.S., & Brown, H.R. (1996). Frontal lobe injuries, violence, and aggression: A report of the Vietnam head injury study. *Neurology, 46,* 1231–1238.

Gregg, T.R., & Siegel, A. (2001). Brain structures and neurotransmitters regulating aggression in cats: Implications for human aggression. *Progress in Neuropsychopharmacology and Biological Psychiatry, 25,* 91–140.

Guy, J.D., Majorski, L.V., Wallace, C.J., & Guy, M.P. (1983). The incidence of minor physical anomalies in adult male schizophrenics. *Schizophrenia Bulletin, 9,* 571–582.

Hare, R.D. (1970). *Psychopathy: Theory and research.* New York: Wiley.

Hare, R.D. (1980). A research scale for the assessment of psychopathy in criminal populations. *Personality and Individual Differences, 1,* 111–119.

Hare, R.D. (1991). *The Hare Psychopathy Checklist-Revised.* Toronto, Ontario: Multi-Health Systems.

Harmer, C.J., Perrett, D.I., Cowen, P.J., & Goodwin, G.M. (2001). Administration of the betaadrenoceptor blocker propranolol impairs the processing of facial expressions of sadness. *Psychopharmacology (Berl), 154,* 383–389.

Hart, S.D., & Hare, R.D. (1996). Psychopathy and antisocial personality disorder. *Current Opinion in Psychiatry, 9,* 129–132.

Herpertz, S.C., Werth, U., Lukas, G., Qunaibi, M., Schuerkens, A., Kunert, H.J., et al. (2001). Emotion in criminal offenders with psychopathy and borderline personality disorder. *Archives of General Psychiatry, 58,* 737–745.

Hiatt, K.D., Schmitt, W.A., & Newman, J.P. (2004). Stroop tasks reveal abnormal selective attention

among psychopathic offenders. *Neuropsychology*, *18*, 50–59.

Hodgins, S., Kratzer, L., & McNeil, T.F. (2001). Obstetric complications, parenting, and risk of criminal behavior. *Archives of General Psychiatry*, *58*, 746–752.

Hodgins, S., Kratzer, L., & McNeil, T.F. (2002). Obstetrical complications, parenting practices and risk of criminal behaviour among persons who develop major mental disorders. *Acta Psychiatrica Scandinavica*, *105*, 179–188.

Kandel, E., & Freed, D. (1989). Frontal lobe dysfunction and antisocial behavior: A review. *Journal of Clinical Psychology*, *45*, 404–413.

Kiehl, K.A. (in press). A paralimbic dysfunction hypothesis of psychopathy. In D. Barch (Ed.), *Cognitive and affective neuroscience of psychopathology*. London, UK: Oxford University Press.

Kiehl, K.A., Smith, A.M., Hare, R.D., Mendrek, A., Forster, B.B., Brink, J., et al. (2001). Limbic abnormalities in affective processing by criminal psychopaths as revealed by functional magnetic resonance imaging. *Biological Psychiatry*, *50*, 677–684.

King, S.M. (1999). Escape-related behaviours in an unstable, elevated and exposed environment. II. Long-term sensitization after repetitive electrical stimulation of the rodent midbrain defence system. *Behavioral Brain Research*, *98*, 127–142.

Kochanska, G. (1997). Multiple pathways to conscience for children with different temperaments: From toddlerhood to age 5. *Developmental Psychology*, *33*, 228–240.

LaBar, K.S., LeDoux, J.E., Spencer, D.D., & Phelps, E.A. (1995). Impaired fear conditioning following unilateral temporal lobectomy in humans. *Journal of Neuroscience*, *15*, 6846–6855.

LaPierre, D., Braun, C.M.J., & Hodgins, S. (1995). Ventral frontal deficits in psychopathy: Neuropsychological test findings. *Neuropsychologia*, *33*, 139–151.

Levenston, G.K., Patrick, C.J., Bradley, M.M., & Lang, P.J. (2000). The psychopath as observer: Emotion and attention in picture processing. *Journal of Abnormal Psychology*, *109*, 373–386.

Lilienfeld, S.O., & Andrews, B.P. (1996). Development and preliminary validation of a self-report measure of psychopathic personality traits in noncriminal populations. *Journal of Personality Assessment*, *66*, 488–524.

Lorenz, A.R., & Newman, J.P. (2002). Deficient response modulation and emotion processing in low anxious Caucasian psychopathic offenders: Results from a lexical decision task. *Emotion*, *2*, 91–104.

Lovelace, L., & Gannon, L. (1999). Psychopathy and depression: Mutually exclusive constructs? *Journal of Behavioral Therapy and Experimental Psychiatry*, *30*, 169–176.

Luria, A. (1966). *Higher cortical functions in man*. New York: Basic Books.

Lykken, D.T. (1957). A study of anxiety in the sociopathic personality. *Journal of Abnormal and Social Psychology*, *55*, 6–10.

Lykken, D.T. (1995). *The antisocial personalities*. Hillsdale, NJ: Erlbaum.

MacDonald, E., & Scheinin, M. (1995). Distribution and pharmacology of alpha 2-adrenoceptors in the central nervous system. *Journal of Physiology and Pharmacology*, *46*, 241–258.

Mednick, S.A., & Kandel, E.S. (1988). Congenital determinants of violence. *Bulletin of the American Academy of Psychiatry and Law*, *16*, 101–109.

Miles, D.R., & Carey, G. (1997). Genetic and environmental architecture of human aggression. *Journal of Personality and Social Psychology*, *72*, 207–217.

Miller, J.D., Flory, K., Lynam, D.R., & Leukefeld, C. (2003). A test of the four-factor model of impulsivity-related traits. *Personality and Individual Differences*, *34*, 1403–1418.

Miller, L.S., Wasserman, G.A., Neugebauer, R., Gorman-Smith, D., & Kamboukos, D. (1999). Witnessed community violence and antisocial behavior in high-risk, urban boys. *Journal of Clinical Child Psychology*, *28*, 2–11.

Mitchell, D.G.V., Colledge, E., Leonard, A., & Blair, R.J.R. (2002). Risky decisions and response reversal: Is there evidence of orbitofrontal cortex dysfunction in psychopathic individuals? *Neuropsychologia*, *40*, 2013–2022.

Mitchell, D.G.V., Richell, R.A., Leonard, A., & Blair, R.J.R. (in press). Emotion at the expense of cognition: Psychopathic individuals outperform controls on an operant response task. *Journal of Abnormal Psychology*.

Moffitt, T.E. (1993). Adolescence-limited and life-course-persistent antisocial behavior: A developmental taxonomy. *Psychological Review*, *100*, 674–701.

Morgan, A.B., & Lilienfield, S.O. (2000). A meta-analytic review of the relation between antisocial behavior and neuropsychological measures of executive function. *Clinical Psychology Review*, *20*, 113–136.

Morris, J.S., Frith, C.D., Perrett, D.I., Rowland, D., Young, A.W., Calder, A.J., et al. (1996). A differential response in the human amygdala to fearful and happy facial expressions. *Nature*, *383*, 812–815.

Muller, J.L., Sommer, M., Wagner, V., Lange, K., Taschler, H., Roder, C.H., et al. (2003). Abnormalities in emotion processing within cortical and subcortical regions in criminal psychopaths: Evidence from a functional magnetic resonance imaging study using pictures with emotional content. *Biological Psychiatry*, *15*, 152–162.

Newman, J.P. (1998). Psychopathic behaviour: An information processing perspective. In D.J. Cooke, A.E. Forth, & R.D. Hare (Eds.), *Psychopathy: Theory, research and implications for society* (pp. 81–105). Dordrecht, The Netherlands: Kluwer Academic Publishers.

Newman, J.P., & Kosson, D.S. (1986). Passive avoidance learning in psychopathic and nonpsychopathic offenders. *Journal of Abnormal Psychology*, *95*, 252–256.

Newman, J.P., Patterson, C.M., & Kosson, D.S. (1987). Response perseveration in psychopaths. *Journal of Abnormal Psychology*, *96*, 145–148.

O'Doherty, J.P., Dayan, P., Friston, K., Critchley, H., & Dolan, R.J. (2003). Temporal difference models and reward-related learning in the human brain. *Neuron*, *38*, 329–337.

Oxford, M., Cavell, T.A., & Hughes, J.N. (2003). Callous-unemotional traits moderate the relation between ineffective parenting and child externalizing problems:

A partial replication and extension. *Journal of Clinical Child and Adolescent Psychology*, *32*, 577–585.

Panksepp, J. (1998). *Affective neuroscience: The foundations of human and animal emotions.* New York: Oxford University Press.

Passingham, R.E., & Toni, I. (2001). Contrasting the dorsal and ventral visual systems: Guidance of movement versus decision making. *Neuroimage, 14,* S125–S131.

Patrick, C.J. (1994). Emotion and psychopathy: Startling new insights. *Psychophysiology, 31,* 319–330.

Patrick, C.J., Bradley, M.M., & Lang, P.J. (1993). Emotion in the criminal psychopath: Startle reflex modulation. *Journal of Abnormal Psychology, 102,* 82–92.

Patterson, C.M., & Newman, J.P. (1993). Reflectivity and learning from aversive events: Toward a psychological mechanism for the syndromes of disinhibition. *Psychological Review, 100,* 716–736.

Pennington, B.F., & Bennetto, L. (1993). Main effects or transaction in the neuropsychology of conduct disorder? Commentary on 'The neuropsychology of conduct disorder'. *Development and Psychopathology, 5,* 153–164.

Peschardt, K.S., Morton, J., Blair, R.J.R. (under revision). They know the words but don't feel the music: Reduced affective priming in psychopathic individuals..

Peschardt, K.S., Morton, J., Leonard, A., & Blair, R.J.R. (in press a). Impaired decision-making on the basis of both reward and punishment information in individuals with psychopathy. *Personality and Individual Differences.*

Peschardt, K.S., Newman, C., Mitchell, D.G.V., Richell, R.A., Leonard, A., Morton, J., et al. (in press b). Differentiating among prefrontal substrates in psychopathy: neuropsychological test findings. *Neuropsychology.*

Pine, D.S., Shaffer, D., Schonfeld, I.S., & Davies, M. (1997). Minor physical anomalies: Modifiers of environmental risks for psychiatric impairment? *Journal of the American Academy of Child and Adolescent Psychiatry, 36,* 395–403.

Piquero, A., & Tibbetts, S. (1999). The impact of pre/perinatal disturbances and disadvantaged familial environment in predicting criminal offending. *Studies on Crime and Crime Prevention, 8,* 52–70.

Raine, A. (1993). *The psychopathology of crime: Criminal behavior as a clinical disorder.* San Diego, CA: Academic Press.

Raine, A. (2002a). Annotation: The role of prefrontal deficits, low autonomic arousal, and early health factors in the development of antisocial and aggressive behavior in children. *Journal of Child Psychology and Psychiatry, 43,* 417–34.

Raine, A. (2002b). Biosocial studies of antisocial and violent behavior in children and adults: A review. *Journal of Abnormal Child Psychology, 30,* 311–326.

Raine, A., Brennan, P., & Mednick, S.A. (1994). Birth complications combined with early maternal rejection at age 1 year predispose to violent crime at age 18 years. *Archives of General Psychiatry, 51,* 984–988.

Raine, A., Meloy, J.R., Birhle, S., Stoddard, J., LaCasse, L., & Buchsbaum, M.S. (1998). Reduced prefrontal and increased subcortical brain functioning assessed using positron emission tomography in predatory and affective murderers. *Behaviour Science and Law, 16,* 319–332.

Rhee, S.H., & Waldman, I.D. (2002). Genetic and environmental influences on antisocial behavior: a meta-analysis of twin and adoption studies. *Psychological Bulletin, 128,* 490–529.

Rogeness, G.A., Cepeda, C., Macedo, C.A., Fischer, C., & Harris, W.R. (1990). Differences in heart rate and blood pressure in children with conduct disorder, major depression, and separation anxiety. *Psychiatry Research, 33,* 199–206.

Rogers, R.D., Lancaster, M., Wakeley, J., & Bhagwager, Z. (submitted). The effects of beta-adrenoceptor blockade on components of human decision-making.

Rolls, E.T. (1997). The orbitofrontal cortex. *Philosophical Transactions of the Royal Society of London B, 351,* 1433–1443.

Rolls, E.T., Hornak, J., Wade, D., & McGrath, J. (1994). Emotion-related learning in patients with social and emotional changes associated with frontal lobe damage. *Journal of Neurology, Neurosurgery, and Psychiatry, 57,* 1518–1524.

Schwab-Stone, M., Chen, C., Greenberger, E., Silver, D., Lichtman, J., & Voyce, C. (1999). No safe haven II: The effects of violence exposure on urban youth. *Journal of the American Academy of Child and Adolescent Psychiatry, 38,* 359–367.

Shallice, T., & Burgess, P.W. (1996). The domain of supervisory processes and temporal organization of behaviour. *Philosophical Transactions of the Royal Society of London B, 351,* 1405–1412.

Silverthorn, P., & Frick, P.J. (1999). Developmental pathways to antisocial behavior: The delayed onset pathway in girls. *Development and Psychopathology, 11,* 101–26.

Soderstrom, H., Blennow, K., Manhem, A., & Forsman, A. (2001). CSF studies in violent offenders. I. 5-HIAA as a negative and HVA as a positive predictor of psychopathy. *Journal of Neural Transmission, 108,* 869–878.

Soderstrom, H., Blennow, K., Sjodin, A.K., & Forsman, A. (2003). New evidence for an association between the CSF HVA:5-HIAA ratio and psychopathic traits. *Journal of Neurology, Neurosurgery and Psychiatry, 74,* 918–921.

Stuss, D.T., Gallup, G.G.J., & Alexander, M.P. (2001). The frontal lobes are necessary for 'theory of mind'. *Brain, 124,* 279–286.

Trasler, G.B. (1973). Criminal behaviour. In H.J. Eysenck (Ed.), *Handbook of abnormal psychology* (pp. 67–96). London: Pitman.

Veit, R., Flor, H., Erb, M., Hermann, C., Lotze, M., Grodd, W., et al. (2002). Brain circuits involved in emotional learning in antisocial behavior and social phobia in humans. *Neuroscience Letters, 328,* 233–236.

Verona, E., Curtin, J.J., Patrick, C.J., Bradley, M.M., & Lang, P.J. (2004). Psychopathy and physiological response to emotionally evocative sounds. *Journal of Abnormal Psychology, 113,* 99–108.

Verona, E., Patrick, C.J., & Joiner, T.E. (2001). Psychopathy, antisocial personality, and suicide risk. *Journal of Abnormal Psychology, 110,* 462–470.

Viding, E., Blair, R.J.R., Moffitt, T.E., & Plomin, R. (2005). Evidence for substantial genetic risk for psychopathy in 7-year-olds. *Journal of Child Psychology and Psychiatry*, *46*, 592–597.

Volkow, N.D., Tancredi, L.R., Grant, C., Gillespie, H., Valentine, A., Mullani, N., et al. (1995). Brain glucose metabolism in violent psychiatric patients: A preliminary study. *Psychiatry Research*, *61*, 243–253.

Whiteside, S.P., & Lynam, D.R. (2001). The five factor model and impulsivity: Using a structural model of personality to understand impulsivity. *Personality and Individual Differences*, *30*, 669–689.

Widom, C.S. (1992). *The cycle of violence*. Washington, DC: U.S. Dept. of Justice, Office of Justice Programs, National Institute of Justice.

Williamson, S., Hare, R.D., & Wong, S. (1987). Violence: Criminal psychopaths and their victims. *Canadian Journal of Behavioral Science*, *19*, 454–462.

Williamson, S., Harpur, T.J., & Hare, R.D. (1991). Abnormal processing of affective words by psychopaths. *Psychophysiology*, *28*, 260–273.

Wootton, J.M., Frick, P.J., Shelton, K.K., & Silverthorn, P. (1997). Ineffective parenting and childhood conduct problems: The moderating role of callous-unemotional traits. *Journal of Consulting and Clinical Psychology*, *65*, 292–300.