The amygdala and ventromedial prefrontal cortex: functional contributions and dysfunction in psychopathy

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The current paper examines the functional contributions of the amygdala and ventromedial prefrontal cortex (vmPFC) and the evidence that the functioning of these systems is compromised in individuals with psychopathy. The amygdala is critical for the formation of stimulus–reinforcement associations, both punishment and reward based, and the processing of emotional expressions. vmPFC is critical for the representation of reinforcement expectancies and, owing to this, decision making. Neuropsychological and neuroimaging data from individuals with psychopathy are examined. It is concluded that these critical functions of the amygdala and vmPFC, and their interaction, are compromised in individuals with the disorder. It is argued that these impairments lead to the development of psychopathy.

Keywords: amygdala; ventromedial prefrontal cortex; psychopathy

1. INTRODUCTION
Psychopathy is a developmental disorder (Lynam et al. 2007) marked by emotional dysfunction (reduced guilt and empathy) and antisocial behaviour (Harpur et al. 1988; Hare 1991; Frick 1995). The disorder is not equivalent to the psychiatric diagnoses of conduct disorder (CD) or antisocial personality disorder (DSM-IV) or CD and dissocial personality disorder (ICD-10; for full details on the assessment of psychopathy, see Patrick 2006). These psychiatric diagnoses concentrate on the antisocial behaviour shown by the individual rather than any putative cause such as the emotion dysfunction seen in psychopathy. A distinctive feature of psychopathy is that it confers an increased risk for both reactive and instrumental aggression (Cornell et al. 1996; Frick et al. 2003). Reactive aggression is triggered by a frustrating or threatening event and involves unplanned enraged attacks on the object perceived to be the source of the threat/frustration. This aggression type is often accompanied by anger and can be considered ‘hot’. Importantly, it is initiated without regard for any potential goal. This is in direct contrast with instrumental aggression, which is purposeful and goal directed (e.g. to obtain the victim’s possessions). Furthermore, instrumental aggression need not be accompanied by an emotional state, such as anger, and can be considered ‘cold’. Many emotional disorders conditions (e.g. childhood bipolar disorder, post-traumatic stress disorder) confer an increased risk for reactive aggression (Blair et al. 2005). However, psychopathy is the only psychiatric condition to also confer an increased risk for instrumental aggression.

The goal of this review is to consider the cognitive neuroscience of psychopathy. In short, the functional contributions of two core neural systems, evidence of their dysfunction in psychopathy and the developmental consequences of these dysfunctions will be considered. In this review, the primary causes of the disorder, i.e. the contribution of genes and the environment, will not be considered in detail. However, the strong suggestion here is that there is a genetic contribution to the emotion dysfunction, which is the core of psychopathy and also described in this paper. Currently, there are no known environmental factors (including trauma and neglect) that can give rise to the pathophysiology seen in psychopathy (see Blair 2007). Instead, these environmental factors are associated with increased responsiveness in the amygdala in particular (see Blair 2007) rather than the decreased responsiveness seen in psychopathy (see below). This, of course, does not imply that social and environmental factors have no impact on the development of the disorder. Indeed, it will be argued below that they have a significant impact on how the disorder manifests in the individual.

The two core neural systems that will be considered in this paper are the amygdala and ventromedial prefrontal cortex (vmPFC). The term ‘amygdala’ was first used by Burdach (1819–1822) to describe an almond-shaped mass of grey matter in the anterior portion of the human temporal lobe. Later work subdivided the amygdala into distinct nuclei with a primary division being made between the basolateral

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and central nuclei (Johnston 1923), a division that remains in the literature today. For the purposes of this paper, vmPFC is considered to include Brodmann’s areas 10 and 11 and the inferior regions of rostral anterior cingulate cortex and subgenual cingulate cortex (BA 32 and 24). The regions of vmPFC have considerable interconnectivity with the amygdala (Price 2003).

2. FUNCTIONS OF THE AMYGDALA AND vmPFC

(a) The amygdala

The goal here is not to provide a complete overview on the functions of the amygdala and vmPFC but rather to describe those functions implicated in understanding psychopathy. The amygdala is involved in stimulus–reinforcement learning. At one stage, the general view was that the basolateral nuclei received sensory input and allowed the formation of conditioned stimulus–unconditioned stimulus associations. These associations then allowed the basolateral amygdala to control the activity of the central nucleus, which in turn allowed the control of hypothalamic and brainstem structures to orchestrate behavioural, autonomic and neuroendocrine responses (LeDoux 1998; Davis 2000). However, it is now clear that the basolateral amygdala does more than control the central nucleus (Everitt et al. 2003; Schoenbaum & Roesch 2005). In particular, it allows the transmission of stimulus–reinforcement association information and reinforcement expectancies forward to vmPFC for appropriate decision making (see below; Schoenbaum & Roesch 2005).

Much work has stressed the role of the amygdala with respect to aversive conditioning (LeDoux 1998; Buchel & Dolan 2000; Davis 2000). However, it is now clear that the amygdala also plays a role in appetitive conditioning (Gottfried et al. 2002; Everitt et al. 2003). Moreover, the amygdala plays a role in instructed fear, showing greater responsiveness to stimuli that subjects have been simply told will anticipate shock (Phelps et al. 2001). Presumably, the instructed fear stimulus is semantically associated with conditioned stimuli and thus comes to activate the amygdala.

Aversive and appetitive conditioning involves the interaction of temporal cortex and the amygdala (LeDoux 1998). Conditioned stimuli, represented within temporal cortex, become associated with valence information represented within the amygdala. As the connections between temporal cortex and the amygdala are reciprocal (Amaral et al. 1992), the activity of neurons representing emotional stimuli in temporal cortex is further augmented by reciprocal feedback from the amygdala. Emotional attention can be understood in terms of this interaction between the temporal cortex and the amygdala (Pessoa & Ungerleider 2004; Mitchell et al. 2006). Representations of emotional stimuli in temporal cortex are primed by the amygdala as a function of the degree to which they activate the amygdala. As such, emotional distractors should and do cause greater interference on task performance than neutral distractors (Erthal et al. 2005; Mitchell et al. 2006; Blair et al. 2007). Conversely, if the emotional stimulus is relevant to task performance, then there will be facilitation of performance relative to neutral stimuli. This can be seen in emotional lexical decision paradigms where healthy volunteers are usually significantly faster/more accurate to judge that emotional letter strings (e.g. ‘murder’) are words rather than neutral letter strings (e.g. ‘table’; Graves et al. 1981; Lorenz & Newman 2002; Nakic et al. 2006).

Considerable data indicate that the amygdala is involved in the processing of emotional expressions (for reviews, see Adolphs 2002; Blair 2003). However, there are two issues that remain open to debate. The first of these concerns which expressions the amygdala responds to. There have been suggestions that the amygdala responds to all emotional expressions (Winston et al. 2003; Fitzgerald et al. 2006). However, a considerable number of other studies have not supported this view (Morris et al. 1996; Blair et al. 1999; LaBar et al. 2003). Moreover, a meta-analysis of the literature strongly supported the suggestion that the amygdala is particularly responsive to fearful expressions (Murphy et al. 2003).

The second, related issue concerns the nature of the function of the amygdala’s response to expression information. One influential view suggests that the ‘amygdala monitors the environment for stimuli that signal an increased probability of threat’ and that the ‘magnitude of amygdala activation may be inversely related to the amount of information concerning the nature of the threat’ (Whalen 1998, p. 180). According to this view, fearful faces are innately specified threat stimuli that ‘engage the amygdala to a greater degree than angry faces because they require more information concerning the nature of a probable threat’ (Whalen 1998, p. 180). Fearful expressions are considered more ambiguous threats than angry expressions because they provide less information regarding the source of the threat and thus lead to increased amygdala activity.

A second view suggests that fearful faces should be viewed as ‘reinforcers that modulate the probability that a particular behaviour will be performed in the future’ and this function as reinforcers lead to amygdala activity (Blair 2003, p. 564). By contrast, angry expressions are considered to ‘serve to inform the observer to stop the current behavioural action’ and ‘can be seen as triggers for response reversal’ (Blair 2003, p. 564). In line with this position, angry faces have been shown to activate the regions of inferior frontal cortex (Murphy et al. 2003). This region is consistently implicated in reversal learning (Cools et al. 2002; Budhani et al. 2007).

A recent study by Hooker et al. (2006) allowed a direct contrast of these views. In this study, healthy participants were presented with images of individuals displaying fearful and happy expressions either towards novel objects (i.e. probable threats) or empty space (i.e. no information was provided regarding the nature of the threat). If amygdala activation was inversely related to the amount of information regarding the nature of the threat (i.e. related to increased ambiguity), then there should be greater activation to the fearful expression when presented alone, relative to when it was presented as a response to an object. Alternatively, if the amygdala treats particular expressions as
reinforcers (i.e. cues to stimulus–reinforcement learning), then the amygdala should show greater activity when there were object stimuli to associate with the expression reinforcement. The data clearly supported the latter suggestion; there was significantly greater amygdala activity when there were object stimuli to associate with the expression reinforcement (Hooker et al. 2006, p. 8915). In short, and as noted by Hooker and colleagues, the data indicated that the ‘amygdala uses social signals to rapidly and flexibly learn threatening and rewarding associations’.

(b) The vmPFC

Much of the clinical neuroscience literature stresses a role for vmPFC in emotional regulation (Phillips et al. 2003; Rauch et al. 2006). Thus, animal work has shown that train stimulation of medial prefrontal cortex in rats suppresses neuronal activity in the basolateral nucleus of the amygdala otherwise seen to conditioned stimuli (Rosenkranz et al. 2003). However, which regions of vmPFC are involved in emotional regulation in humans remains unclear. Rostral anterior cingulate cortex has frequently been implicated (Whalen et al. 1998; Pezawas et al. 2005; Etkin et al. 2006) with subgenual anterior cingulate cortex appearing to be in receipt of emotional information from the amygdala (Pezawas et al. 2005; Budhani et al. 2007) and supragenual cingulated cortex acting to suppress the amygdala (Pezawas et al. 2005; Etkin et al. 2006). In our own work, we have observed activity in a slightly lateral polar region of vmPFC in tasks requiring the suppression of emotional distracter information (Blair et al. 2007; Mitchell et al. 2007). This region has also been typically activated in tasks where participants are explicitly instructed to suppress their emotional reactions (Beauregard et al. 2001; Ohira et al. 2006).

While some regions of vmPFC are involved in emotional regulation, it is important to note that vmPFC, as articulated above, is a large area that is probably implicated in a variety of functions. Considerable data indicate a role for vmPFC in encoding reinforcement outcome information (Knutson & Cooper 2005; Schoenbaum & Roesch 2005; Rushworth et al. 2007). Indeed, vmPFC appears to receive reinforcement expectation information in stimulus–reinforcement-based instrumental learning paradigms (such as the animal go/no-go task—referred to in the human literature as the passive avoidance learning paradigm). The availability of this information is critical for appropriate decision making (Schoenbaum & Roesch 2005; Kosson et al. 2006). Moreover, vmPFC lesions actually diminish reinforcement-expectancy activity in the basolateral nucleus of the amygdala (Schoenbaum et al. 2003), i.e. suppression is not the only interaction that vmPFC has with the amygdala.

Considerable progress has been made on the functional contributions of vmPFC. Suggestions have been made that orbitofrontal cortex (OFC) normalizes the value of competing outcomes so that the value of differing rewards such as apples and oranges can be compared (Montague & Berns 2002; Schoenbaum & Roesch 2005). In line with these suggestions, recent recording work demonstrated the existence of cells in OFC that encode the value of offered and chosen goods. They show greater activity to smaller amounts of a more desirable object relative to greater amounts of a less desirable object (Padoa-Schioppa & Assad 2006).

Interestingly, while vmPFC is importantly involved in the representation of value information crucial for stimulus selection, this region itself does not appear to directly select between responses. There had been suggestions that vmPFC was involved in the comparison of values and stimulus selection (Arana et al. 2003; Blair 2004; Schoenbaum & Roesch 2005). However, such suggestions made clear predictions: if vmPFC is involved in the comparison of values, it should show differential responsiveness to parameters that increase choice difficulty on the basis of value information. We examined two such parameters on vmPFC activity: (i) the degree of difference in reinforcement associated with the chosen and non-chosen objects (the greater the differential in value, the easier the decision making; Blair et al. 2006b) and (ii) the number of objects to choose between (the fewer objects with different values to choose between, the easier the decision making; Marsh et al. 2007). In both the Blair et al. (2006b) and Marsh et al. (2007) studies, vmPFC activity was seen to vary as a function of the reinforcement associated with the chosen stimulus. However, vmPFC activity was not influenced by either the degree of difference in reinforcement associated with the chosen and non-chosen objects (Blair et al. 2006b) or the number of objects to choose between (Marsh et al. 2007). In short, vmPFC is importantly involved in the representation of value information but does not directly select between responses.

It appears plausible that dorsomedial prefrontal cortex may be operating on the translation of reinforcement-expectancy information into response tendencies to mediate response selection. Considerable work has demonstrated a role for dorsomedial prefrontal cortex in the monitoring and resolution of response conflict (Cohen et al. 2000; Botvinick et al. 2004). If reinforcement expectancies are translated as approach or avoidance tendencies, then response options that are close in reinforcement value should be associated with similar strength approach or avoidance tendencies and greater response conflict (cf. Blair et al. 2006b). Similarly, the greater the number of response options, the greater should be the response conflict (cf. Marsh et al. 2007). Certainly, dorsal regions of anterior cingulate cortex did show significant activity in response to both the degree of difference in reinforcement associated with the chosen and non-chosen objects and the number of objects to choose between (Blair et al. 2006b; Marsh et al. 2007).

On a related note, vmPFC has been consistently implicated in reversal learning in animal (Iversen & Mishkin 1970; Dias et al. 1996; Izquierdo et al. 2004) and some human work (Fellows & Farah 2003; O’Doherty et al. 2003; Budhani et al. 2007). During reversal learning, vmPFC shows a significant reduction in activity during reversal errors (trials when a previously rewarded response is now punished; Budhani et al. 2007). It is possible that this signalling in vmPFC may be needed for the detection of contingency change and thus the initiation of reversal learning (Budhani et al. 2007). Alternatively, vmPFC

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may orchestrate reversal learning by representing the reinforcement associated with the two responses. VmPFC appears to track the expectation of reinforcement associated with not only chosen but also non-chosen objects (Blair et al. 2006b; Hampton et al. 2006; Padoa-Schioppa & Assad 2006). It has been argued that vmPFC may increase the representation of reward expectancy associated with the non-chosen object if the chosen object does not elicit reward (Hampton et al. 2006). By this latter account, as the old correct response becomes more frequently punished, the expectancy of reward associated with it decreases. At the same time, the expectancy of reward associated with the new correct response increases. When the expectancy of reward associated with the new correct response is greater than the expectancy of reward associated with the old correct response, the participant should switch their responding (cf. Hampton et al. 2006).

3. THE COGNITIVE NEUROSCIENCE OF PSYCHOPATHY: AMYGDALA AND vmPFC DYSFUNCTION

In §2, the core functions of the amygdala and vmPFC that are believed to be of core relevance to the understanding of psychopathy have been described. In this section, the data indicating amygdala and vmPFC dysfunction in psychopathy will be considered.

(a) Amygdala dysfunction

As noted above, a considerable literature implicates the amygdala in stimulus–reinforcement association formation (LeDoux 1998; Buchel & Dolan 2000; Davis 2000). Individuals with psychopathy show pronounced impairment on tasks reliant on the ability to form stimulus–reinforcement associations. For example, some of the earliest findings in psychopathy were demonstrations of the impairment in aversive conditioning (Lykken 1957; Hare 1970). Moreover, recent functional magnetic resonance imaging (fMRI) work has shown that individuals with psychopathy show reduced amygdala activity during aversive conditioning (Birbaumer et al. 2005). Related to this function, the amygdala allows conditioned stimuli to prime brainstem threat circuits mediating the startle reflex such that a startle probe elicits greater startle after a threatening prime relative to a neutral prime (Davis 2000). Individuals with psychopathy do not show appropriate augmentation of the startle reflex following a negative prime (Patrick et al. 1993; Levenston et al. 2000). The amygdala also plays a role in instructed fear, when subjects are told that a stimulus is associated with shock (Phelps et al. 2001). Individuals with psychopathy show reduced autonomic responses, relative to comparison individuals, to instructed fear cues (e.g. Hare et al. 1978).

In the above paragraph, emotional attention to stimulus–reinforcement learning and the consequent interaction between the temporal cortex and the amygdala has been related (Pessoa & Ungerleider 2004; Mitchell et al. 2006). If there is amygdala dysfunction in psychopathy, individuals with the disorder should show significantly less interference by emotional distractors. Two studies have directly examined this issue (Christianson et al. 1996; Mitchell et al. 2006). Christianson et al. (1996) showed that emotional, relative to neutral, content in images caused significantly less interference with the recollection of non-emotional peripheral content in individuals with psychopathy relative to comparison individuals. Mitchell et al. (2006) reported significantly less interference in motor responding in individuals with psychopathy from emotional distracters presented immediately before and after the very rapidly presented target stimuli. A second prediction of amygdala dysfunction in psychopathy with respect to emotional attention is that if the emotional stimulus is relevant to task performance, then individuals with the disorder should show less facilitation by emotional targets. In line with this prediction, individuals with psychopathy show significantly less facilitation by emotional words relative to comparison individuals on the emotional lexical decision task (Williamson et al. 1991; Lorenz & Newman 2002).

fMRI data can also reveal the priming of emotional representations in temporal cortex by reciprocal amygdala activation (i.e. emotional attention). Thus, several studies have shown heightened fusiform/temporal cortex responses to emotional relative to neutral expressions, presumably as a consequence of reciprocal feedback of the amygdala to this region of temporal cortex (Mitchell et al. 2007). Studies examining expression processing in both adults with psychopathy (Deeley et al. 2006) and children with psychopathic traits have shown a reduced differential response within fusiform cortex to fearful relative to neutral expressions. These data are consistent with reduced priming of emotion relevant representations in temporal cortex by reciprocal amygdala activation in individuals with psychopathy (though only observed reduced amygdala activity). In addition, a recent work has shown that patients with amygdala lesions show (i) reduced eye gaze to the eye region, (ii) that this is related to their impairment in fearful face recognition, and (iii) that attentional instructions to focus on the eye region abolish the recognition impairment (Adolphs et al. 2005). Similarly, recent work by Dadds and colleagues have reported reduced eye gaze to the eye region in children with psychopathic tendencies and that attentional instructions to focus on the eye region abolish their recognition impairment (Dadds et al. 2006). In short, children with psychopathic tendencies show similar emotional attention-related impairments as patients with amygdala lesions.

As noted above, the amygdala appears particularly responsive to fearful expressions (Murphy et al. 2003). While multiple studies have shown specific impairments in fearful expression processing in individuals with psychopathic tendencies (Blair et al. 2004; Montagne et al. 2005; Dadds et al. 2006), not all studies have reported such deficits (Kosson et al. 2002; Glass & Newman 2006). However, a recent meta-analysis of 20 studies examining expression recognition in psychopathy and other instrumentally aggressive populations demonstrated a robust link between these antisocial populations and specific deficits in recognizing fearful expressions (Marsh & Blair 2008). Moreover, imaging
work in subclinical adult populations (Gordon et al. 2004) and children with psychopathic tendencies (Marsh et al. 2008) has reported reduced amygdala responses to fearful expressions in individuals with psychopathic tendencies.

(b) VmPFC dysfunction
As noted above, the amygdala feeds forward reinforcement information associated with stimuli to vmPFC, which then represents this outcome information (Schoenbaum & Roesch 2005). Given the indications of amygdala dysfunction described above, it can be expected that individuals with psychopathy will show anomalous vmPFC activity in response to amygdala activation. Indeed, in the fMRI study of fearful expression processing, Marsh et al. (2008) reported reduced functional connectivity between the amygdala and the vmPFC in the children with psychopathic tendencies relative to the comparison children. Moreover, Birbaumer et al. (2005) reported reduced vmPFC activity as well as reduced amygdala activity in individuals with psychopathy during aversive conditioning (Birbaumer et al. 2005). Similarly, a study examining performance on the prisoner’s dilemma in a subclinical population found reduced amygdala and vmPFC differentiation in the individuals with psychopathic tendencies in BOLD response when making cooperation relative to defection choices (Rilling et al. 2007). In addition, a study of emotional memory reported reduced amygdala and vmPFC responses to emotional words in individuals with psychopathy (Kiehl et al. 2001).

The suggestion is that the reinforcement-expectancy information is critical for optimal decision making (Montague & Berns 2002; Schoenbaum & Roesch 2005). In line with this, vmPFC lesions have been demonstrated to show impairment in decision making (Bechara et al. 2000). Moreover, this impairment on the Iowa gambling task is also relevant on appropriate amygdala functioning (Bechara et al. 1999), as would be predicted given the amygdala’s role in feeding forward reinforcement-expectancy information to vmPFC. Individuals with psychopathy show impairment on the Iowa gambling task (Blair et al. 2001; Mitchell et al. 2002) as do subclinical populations with psychopathic tendencies (van Honk et al. 2002). Neuroimaging data have confirmed that other stimulus–reinforcement-based decision-making tasks such as the passive avoidance learning task (Kosson et al. 2006) and the differential reward-punishment task (Blair et al. 2006b) are also reliant on integrated amygdala–vmPFC activity. Individuals with psychopathy show impairment on both these tasks (Newman & Kosson 1986; Blair et al. 2004; Blair et al. 2006a).

The role of vmPFC in the representation of reinforcement expectancies is also crucial for behavioural extinction and reversal learning in either prediction error signalling (Budhani et al. 2007) or tracking the reinforcement associated with the non-chosen object (Hampton et al. 2006; see above). Individuals with psychopathy are impaired in both behavioural extinction (Newman et al. 1987) and reversal learning (Mitchell et al. 2002; Budhani & Blair 2005; Budhani et al. 2006). Moreover, neuroimaging data from children with psychopathic tendencies performing a reversal learning paradigm have recently been obtained (Finger et al. 2008). In this study, children with psychopathic tendencies and comparison children performed a probabilistic reversal learning paradigm similar to that described by Budhani et al. (2007). They have shown that healthy adults showed a reduced BOLD response within vmPFC to punished incorrect reversal phases responses relative to correct responses. This was consistent with the suggestion that vmPFC was responding to the prediction error, the failure to receive the anticipated reward. In the Finger et al. (2008) study, the comparison children also showed significant reductions in BOLD responses in vmPFC to punished incorrect reversal responses relative to correct responses. By contrast, the children with psychopathic tendencies did not.

The human neuroimaging literature has consistently implicated inferior and dorsomedial prefrontal cortex in reversal learning; both regions show greater BOLD responses to punished reversal errors relative to rewarded correct responses (Cools et al. 2002; Kringlebach & Rolls 2003; Budhani et al. 2007). Interestingly, while children with psychopathic tendencies did not show the appropriate reduction in BOLD response to punished incorrect reversal phase responses relative to correct responses in vmPFC, they did show increases in BOLD response, equivalent to comparison children, in inferior and dorsomedial prefrontal cortex to the same contrast (Finger et al. 2008). This is important because it indicates that any vmPFC detection of reinforcement contingency changes cannot be responsible for the recruitment of dorsomedial and inferior frontal cortex to effect a change in response (cf. Budhani et al. 2007). Indeed, these data suggest a degree of independence in these functional processes. Importantly, there are many cues for error detection that do not rely on a reinforcement-based prediction error signal (cf. Holroyd et al. 2004). It appears that children with psychopathic tendencies are sensitive to such cues and successfully recruit regions necessary for response change accordingly.

In this context, it is worth noting the behavioural performance of adults with psychopathy on reversal learning paradigms (Budhani et al. 2006). Following a punished incorrect response, adults with psychopathy are as likely to change their response on the subsequent trial as comparison individuals. This was not readily accounted for in the Budhani et al. (2006) study. However, the findings of Finger et al. (2008) showing appropriate recruitment of dorsomedial and inferior frontal cortex to punished reversal errors perhaps provide an explanation.

It can be assumed that reinforcement information, in the context of reversal learning and other paradigms, serves two functions: first, it changes the outcome expectancy associated with the stimulus, and second, if it is punishment information, it prompts an immediate change in behaviour. The first function involves vmPFC in the representation of appetitive and aversive outcome information, and the second dorsomedial and inferior frontal cortex in the orchestration of behavioural change (see above). On the basis of both Budhani et al.’s (2006) behavioural and
Finger et al.'s (2008) fMRI results, the second function appears to be intact in psychopathy. Punishment information appropriately activates dorsomedial and inferior frontal cortex (cf. Finger et al. 2008) orchestrating a shift in responding on the immediate subsequent trial (cf. Budhani et al. 2006).

By contrast, the first function, the role of vmPFC in the representation of outcome information, appears to be dysfunctional in psychopathy (cf. Finger et al. 2008). This suggests that response selection on the basis of outcome information should be impaired. Adults with psychopathy show impairment on trials subsequent to a rewarded correct response—they are significantly more likely to revert to the previously rewarded, now no longer correct, response than comparison individuals (Budhani et al. 2006). These are trials that are likely to be particularly under the control of outcome expectancy calculations.

4. CONCLUSIONS: DEVELOPMENTAL CONSEQUENCES OF AMYGDALA AND vmPFC DYSFUNCTION

In §§1–3, the description of the functional contributions of the two core regions that are dysfunctional in psychopathy, and the data indicating dysfunction in the functioning of these regions in individuals with the disorder are presented. In this section, a brief consideration of why this dysfunction may lead to the development of the disorder is provided.

As noted above, the amygdala is crucial for stimulus–reinforcement learning and responding to emotional expressions, particularly fearful expressions that, as reinforcers, are important initiators of stimulus–reinforcement learning. Moreover, the amygdala is involved in the formation of both stimulus–punishment and stimulus–reward associations. Individuals with psychopathy show impairment in stimulus–reinforcement learning (whether punishment or reward based) and responding to fearful and sad expressions. It is argued that this impairment drives much of the syndrome of psychopathy. Stimulus–reinforcement learning is crucial for socialization, for learning that some things are bad to do, and individuals with psychopathy fail to take advantage of standard socialization techniques (Wootton et al. 1997). As such, they are more likely to learn to use antisocial strategies to achieve their goals. The reduced amygdala responding also diminishes empathy-based learning following the witnessing of another’s distress and leads to reduced empathy generally. Finally, the impairment in stimulus–reward learning may relate to the reduced attachment reported in this disorder (Hare et al. 2003); individuals with psychopathy may find their carers to be rewarding stimuli and consequently be less motivated to maintain contact with them.

vmPFC is considered critical for the representation of reinforcement information that can then be used by other structures, such as dorsomedial frontal cortex, to implement behaviour. Impairment in vmPFC functioning means that individuals with psychopathy will show impaired decision making. This will contribute to their disordered lifestyle and may increase the risk for drug abuse. Moreover, because vmPFC is very important for successful decision making, its dysfunction will increase the probability that individuals with the disorder will make less than optimal decisions when attempting to achieve their goals. As such this will increase the risk for frustration and potentially frustration-based reactive aggression.

Can the model described above explain all aspects of psychopathy? The answer is almost certainly not. There are aspects of psychopathy (e.g. the grandiose sense of self, superficial charm), which are not clear developmental consequences of the impairment described above. It will be interesting to determine whether these relate to additional impairments or they are consequences of how the dysfunction described interacts with the individual’s social environment.

Importantly, the above suggests pharmacological treatment strategies. While some pharmacological compounds, such as propranolol, decrease amygdala activity, others, such as yohimbine, increase it. Theoretically, it might be possible to increase the responsiveness of the systems described above such that clinically based socialization strategies (e.g. empathy induction and victim awareness) might allow the individual to form more appropriate associations regarding the distress of others and actions that harm others. In short, it is to be hoped that the increased basic understanding of this disorder may soon be translated into therapeutic strategies that will help the individuals concerned.

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REFERENCES


Bechara, A., Tranel, D. & Damasio, H. 2000 Characterization of the decision-making deficit of patients with ventromedial prefrontal cortex lesions. Brain 123(Pt 11), 2189–2202. (doi:10.1093/brain/123.11.2189)


