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The amygdala and ventromedial prefrontal cortex in morality and psychopathy

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Recent work has implicated the amygdala and ventromedial prefrontal cortex in morality and, when dysfunctional, psychopathy. This model proposes that the amygdala, through stimulus-reinforcement learning, enables the association of actions that harm others with the aversive reinforcement of the victims' distress. Consequent information on reinforcement expectancy, fed forward to the ventromedial prefrontal cortex, can guide the healthy individual away from moral transgressions. In psychopathy, dysfunction in these structures means that care-based moral reasoning is compromised and the risk that antisocial behavior is used instrumentally to achieve goals is increased.

Introduction

Care-based morality can be considered as those forms of moral reasoning that concern actions that harm others. Other forms of moral cognition might exist but these will not be considered in detail here (Box 1). Why do we care whether anyone else is hurt? Perhaps equally importantly, why do some people, individuals with psychopathy, care less?

Here, I make reference to the functional roles of the amygdala and ventromedial prefrontal cortex (vmPFC) in the learning and use of reinforcement expectancies (expectancies of reward or punishment). I argue that (i) the integrated functioning of these systems enables the basics of care-based morality; and (ii) dysfunction within these regions in psychopathy means that reinforcement-based decision making, including moral decision making, is impaired.

An early developmental indication of care-based morality: the moral–conventional distinction

Moral transgressions (e.g. one person hitting another) are defined by their consequences for the rights and welfare of others. Social conventional transgressions are defined as violations of the behavioral uniformities that structure social interactions within social systems (e.g. dressing in opposite gender clothing). Healthy individuals distinguish conventional and moral transgressions in their judgments from the age of 39 months [1] and across cultures [2]. In particular, moral transgressions are judged to be less rule-contingent than are conventional transgressions; individuals are less likely to state that moral, rather than conventional, transgressions are permissible in the absence of prohibiting rules [3].

Early models of moral socialization suggested unitary accounts of social rule learning, stressing, for example, either punishment [4] or cultural transmission [5]. However, such accounts struggle to explain the existence of the moral–conventional distinction [3]. Moreover, the social consequences of moral and conventional transgressions differ; caregivers are more likely to refer transgressors of moral rules to the consequences of their actions for the victim and transgressors of conventional rules to the rules themselves or the sanctions against prohibition [6].

Early discussions of the development of the moral–conventional distinction itself suggested that it emerged as a function of abstract reasoning processes [3]. They made two clear predictions. First, populations with impaired abstract reasoning should fail to develop the moral–conventional distinction. However, no data have been presented in support of this position. Moreover, at least one population with pronounced executive function impairment, children with autism, pass the moral–conventional distinction [7]. Second, populations who show impairment in the development of the moral–conventional distinction should show impairment in abstract reasoning and/or executive dysfunction. Individuals with psychopathy show significantly less of a moral–conventional distinction than do healthy individuals [8]. However, before considering executive dysfunction in this population, I will briefly consider the nature of psychopathy.

Psychopathy

Psychopathy is a developmental disorder [9] that involves emotional dysfunction, characterized by reduced guilt, empathy and attachment to significant others, and antisocial behavior including impulsivity and poor behavioral control [10]. It is not equivalent to the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) psychiatric diagnoses of conduct disorder (CD) and antisocial personality disorder (ASPD), which focus only on the presence of antisocial behavior rather than any form of functional impairment that might be causally related to its emergence.

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Box 1. Multiple moralities?

It seems likely that there are other forms of 'moral' reasoning than care-based morality, and that these rely on overlapping or perhaps independent neurocognitive architectures. These might even be intact in individuals with psychopathy. The two principal possibilities relate to disgust-based moral reasoning and reasoning about conventional transgressions.

Disgust has been considered a powerful emotive force for attitudes towards a variety of transgressions, particularly those concerning sexual activity [51]. It seems likely that we use disgust expressions in social interaction in a similar fashion to our use of fearful expressions. Fearful expressions rapidly communicate to others that the object to which the expression is displayed is threatening [52]. Fearful expressions activate the amygdala, particularly if there is a clear object associated with the expression to enable the initiation of emotional learning [42]. It is likely that disgust expressions initiate taste-aversion learning. Taste-aversion learning is mediated by structures such as the insula, which are activated by disgusted expressions [53]. This suggests that we might learn disgust reactions to particular transgressions following the display of disgust expressions directed towards individuals (or descriptions of individuals) engaged in particular transgressions.

But what about the vmPFC? The vmPFC has a major role in the representation of reinforcement outcomes. Given that there are connections between the insula and the vmPFC, it is plausible that disgust-based valenced outcomes might also be represented in the vmPFC. However, this remains to be empirically demonstrated.

Although there have been isolated reports of impairment in the processing of disgust in individuals with psychopathy [54], this is not typically seen [22,23]. This suggests the possibility that the processing of disgust- and potentially disgust-based moral reasoning might be intact in individuals with psychopathy. If this is shown, it will be clear evidence of dissociation between different forms of emotion-based moral reasoning.

There is already evidence of a dissociation between impaired care-based moral reasoning and intact social conventional reasoning in individuals with psychopathy. Although individuals with psychopathy show impairment in care-based moral reasoning, as indexed by their performance on the moral–conventional distinction task, they seem to be intact in the detection and appropriate rating of more conventional transgressions and *faux pas* [55]. Conventional transgressions elicit anger in observers, and both conventional transgressions and induced anger elicit activity in the ventrolateral prefrontal cortex [56,57]. This region is implicated in altering current behavior, particularly when a prepotent response is already engaged [35]. Current data indicate that this region might not be dysfunctional in individuals with psychopathy.

A distinction has long been drawn between reactive and instrumental aggression [11]. Reactive aggression occurs as an explosive response to threat or frustration and is not goal directed (e.g. road rage) [11]. Instrumental aggression is aggression used to achieve a goal (e.g. a mugging) [11]. Various neurological and psychiatric conditions are at heightened risk for reactive aggression (e.g. acquired sociopathy and childhood bipolar disorder [12,13]). Individuals with psychopathy are remarkable, in that they show an increased risk not only for reactive aggression, but also for instrumental aggression [14]. There is something about psychopathy that increases the risk that the individual will use aggression and other antisocial behaviors, actions that harm others, to achieve their goals.

Psychopathy and morality

Individuals with psychopathy show significantly less of a moral–conventional distinction than do healthy individuals [8]. If the moral–conventional distinction emerged as a function of abstract reasoning processes [3], we might believe that individuals with psychopathy will show impairment in abstract reasoning and/or executive dysfunction. However, no data suggest that they do. Indeed, individuals with psychopathy show executive dysfunction only if the executive function has an affective component [15].

Considerable recent work has suggested the importance of emotional responses for moral development [8,16–19]. A specific version of this view suggests that healthy individuals are predisposed to find the distress of others aversive and that we learn to avoid actions associated with this distress (i.e. acts that harm others) [8]. According to this view, we distinguish between moral and conventional transgressions because only moral transgressions are associated with the distress of others, and this association remains intact whether there is a rule prohibiting the action or not. This position predicts that individuals who show reduced processing of the distress of others should show a reduced moral–conventional distinction. Individuals with psychopathy show reduced autonomic responses to the distress of others [20,21] and reduced recognition of sad and fearful expressions [22,23]. They also, of course, make significantly less of a moral–conventional distinction than do comparison individuals [8].

The above suggests that a factor crucial for care-based moral socialization is appropriate emotional responding to the distress of others. If this is lacking, as is the case in psychopathy, there should be interference with socialization. Individuals with psychopathy are less influenced by parental socialization strategies than are healthy individuals [24]. This suggests, in turn, that neural systems implicated in psychopathy might be importantly involved in moral development.

Dysfunctional neural systems in psychopathy

The neuropsychological literature on psychopathy has identified two core neural regions that seem to be dysfunctional in psychopathy: the amygdala and the vmPFC. Psychopathy is associated with a series of core functional impairments: deficits in aversive conditioning, the augmentation of the startle reflex by visual threat primes and fearful expression recognition. These impairments are also seen following lesions of the amygdala [25]. In addition, psychopathy is associated with problems in response reversal and in tasks such as the Iowa gambling task. These impairments are seen following lesions of the vmPFC [26,27]. However, it is important to recognize that psychopathy is not a neurological condition. Psychopathy is not associated with a lesion to a particular region, nor have all functions mediated by any particular region been shown to be compromised. Indeed, although the above functional impairments associated with amygdala dysfunction are seen in psychopathy, other capacities in which the amygdala seems to be implicated, such as determining an internal state from information provided by the eyes, are intact [25].

The neuroimaging literature on psychopathy has found that individuals with psychopathy show reduced activation of both the amygdala and the rostral anterior cingulate cortex/vmPFC in response to emotional words in the context

of emotional memory paradigms [28] and during aversive conditioning [29]. Work with subclinical populations has found that individuals with psychopathic traits show reduced amygdala responses to emotional expressions [30] and less amygdala and vmPFC differentiation in responding when making cooperation relative to defection choices in a prisoner's dilemma paradigm [31]. The neuroimaging literature on psychopathy has also sometimes implicated other structures – for example, the superior temporal cortex and dorsal anterior cingulate cortex (dACC) [32]. However, these findings remain unsubstantiated by neuropsychological findings (and therefore we cannot be sure that they do not simply reflect reduced input from core regions). For example, impaired Stroop performance would be a clear predictor of dACC dysfunction, but this is not seen in psychopathy [25].

Of course, it is impossible to determine on the basis of these imaging results whether the reduced orbital frontal cortex (OFC)/vmPFC activity reflects dysfunction in this region or simply reduced input to this region from the amygdala. A number of animal studies have stressed the importance of the interaction between the amygdala and the OFC/vmPFC [33]. Damage to the amygdala has a detrimental impact on OFC functioning [33]. However, it is important to note that animal studies also suggest that early amygdala dysfunction disrupts the appropriate development of the OFC and vmPFC [34]. Moreover, molecular candidates with respect to the genetic basis for psychopathy innervate both the amygdala and the OFC and vmPFC (Box 2). It thus seems likely that psychopathy is associated with both amygdala and OFC and vmPFC dysfunction. However, to demonstrate this conclusively, it will be necessary to demonstrate anomalous activity in the OFC and vmPFC in a task which does not implicate the amygdala.

The amygdala, vmPFC and morality

The amygdala and vmPFC are implicated not only in the emergence of psychopathy, but also in moral reasoning. Thus, the amygdale, and particularly the vmPFC, have frequently been identified in neuroimaging studies of moral reasoning [18,19,35] (Figure 1). For example, Greene *et al.* [19] reported increased vmPFC activity in response to personal as opposed to impersonal moral choices, and the difference between these two situations related effectively to the salience of the victim. Similarly, in more recent work, Luo *et al.* [35] demonstrated increased amygdala and vmPFC activity in response to more severe relative to less severe moral transgressions.

The moral reasoning imaging literature has not precisely specified the functional roles of the amygdala and vmPFC [36]. In one of the more formalized accounts [37], it has been argued that the vmPFC is implicated in representing social and emotional structured event complexes (SEC). These SECs are considered to be long-term memories of event sequences that guide the perception and execution of goal-oriented activities, such as going to a concert or giving a dinner party. However, as the authors note [37], the SEC framework does not predict how PFC regions interact with limbic areas and other cortical regions.

Box 2. Social and genetic causes of psychopathy

Definitive answers with respect to the fundamental etiology of psychopathy cannot yet be provided. However, some potential basic causes seem less plausible than others. For example, there have been suggestions that psychopathy might be due to early physical or sexual abuse or neglect [58]. However, studies have examined the impact of such stressors on brain development. Animal studies have shown that neglect and other stressors increase emotional and amygdala responsiveness to threatening stimuli [59,60]. Similarly, in humans, early physical or sexual abuse is a significant risk factor for the emergence of post-traumatic stress disorder (PTSD), which is associated with increased emotional and amygdala responsiveness [61]. Increased emotional and amygdala responsiveness is the opposite of the pathology seen in psychopathy.

Data suggest a genetic contribution to the disorder [62,63]. For example, in a recent large study of ~3500 twin pairs, callous–unemotional traits were shown to be strongly heritable (67% heritability) at both seven and nine years of age [63]. However, an understanding of psychopathy at the molecular genetic level remains in its infancy. Suggestive data are provided by recent investigations of the impact of different genetic polymorphisms on neural and behavioral responding. For example, several studies have reported that individuals who are ll homozygotes for the 5-hydroxytryptamine transporter (*5-HTTLPR*) gene show a significantly reduced amygdala response to emotional expressions relative to those who have the short-form polymorphism of the gene [64]. In addition, such individuals show behavioral impairment on some emotional learning tasks reliant on the amygdala [65]. It is possible that there is an array of genes whose polymorphisms increase or decrease emotional and amygdala responsiveness. The basic genetic risk for psychopathy might emerge if an individual possesses a sufficient number of polymorphisms predisposing towards reduced emotional and amygdala responsiveness.

In short, psychopathy is under considerable genetic influence and has yet to be reliably related to a social basic cause. However, although social factors might not be casual, they do influence its manifestation. For example, socioeconomic status (SES) is associated with the emergence of the full syndrome; it is significantly less likely to appear in individuals of higher SES [66]. Reduced SES does not predispose towards reduced emotional and amygdala responsiveness; indeed, as a factor it is unrelated to the emotional component of psychopathy [67]. However, reduced SES does supply a motive: a lack of finances. Reduced SES increases the risk for antisocial behavior in individuals, including those with psychopathy.

A cognitive neuroscience approach to care-based morality and psychopathy

The amygdala

The amygdala is crucial for stimulus-reinforcement learning [38,39]. This learning enables representations of conditioned stimuli within temporal cortex to be linked to emotional responses mediated by the amygdala and other structures (Figure 2). In short, the amygdala enables the individual to learn the goodness and badness of objects and actions. Moreover, because the relationship between the amygdala and the temporal cortex is reciprocal [40], this learning enables the amygdala to influence attention [41]. In humans and other primates, fearfulness serves as a reinforcer, stimuli associated with expression are avoided, and this type of stimulus-reinforcement learning relies on the amygdala too [42,43].

The argument here is that learning the basics of care-based morality – learning that some actions harm others and because of this are to be avoided – relies on this crucial role of the amygdala in stimulus-reinforcement learning. Because of this, the amygdala is often seen to

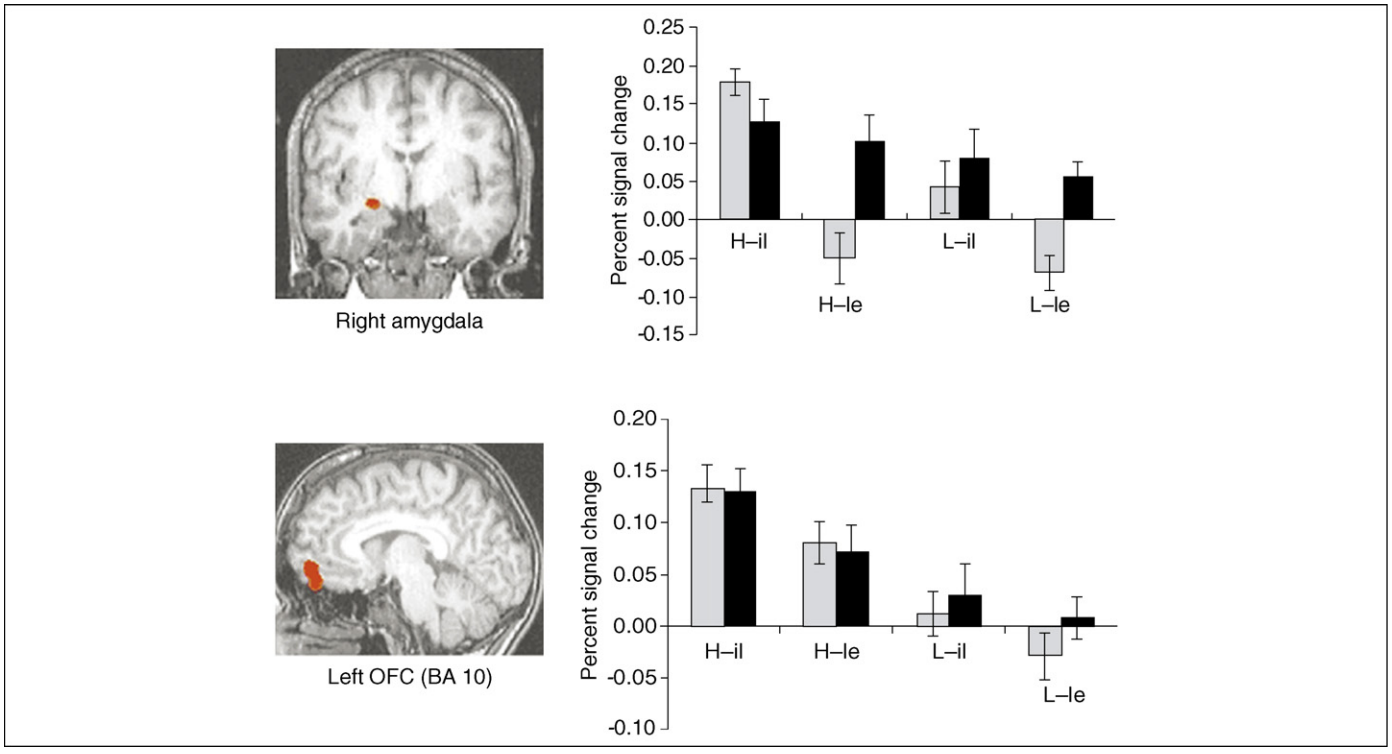

Figure 1. Neural responses to increasing intensity of moral transgressions and positive actions. Both the amygdala and vmPFC show increased activity in response to images of high-intensity illegal content (H-il; scenes of interpersonal violence) and high-intensity legal content (H-le; skydiving) relative to images of low intensity illegal content (L-il; scenes of property damage) and low intensity legal content (L-le; playing the guitar). Reproduced, with permission, from Ref. [35].

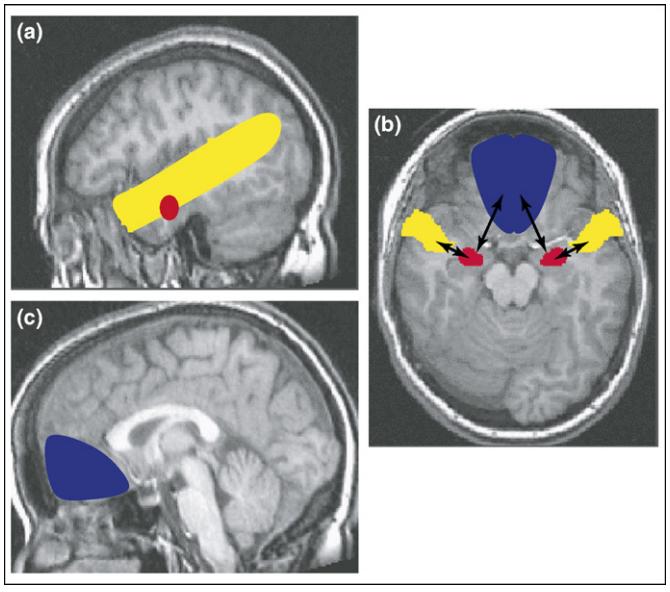

Figure 2. Core brain regions implicated in the basis of care-based morality and, when dysfunctional, psychopathy. These regions include the superior temporal cortex (STC) [**(a,b)**; yellow], the amygdala [(a,b); red] and the vmPFC [**(c,**b); blue]. (b) Stimulus-reinforcement learning enables the association of representations of conditioned stimuli within the temporal cortex, including the STC, to be linked to emotional responses mediated by the amygdala. Of particular importance for care-based morality is associating actions that cause harm with the aversive consequences of the victim's fear and sadness. The connections between the amygdala and temporal cortex are reciprocal, enabling the amygdala to influence attention. Reduced emotion-based attention is seen in psychopathy [70]. The amygdala sends reinforcement expectancy information to the vmPFC. For care-based morality, this is particularly important when the reinforcement expectancy information concerns the anticipated distress of another. This information should guide the healthy information away from the action about to be committed. However, it is argued that reduced information from the amygdale, in addition to dysfunction within the vmPFC in psychopathy, means that this guiding role of the vmPFC functions poorly.

respond in moral reasoning studies [18,44]. Psychopathy represents an extreme case, where aversive conditioning [29] and the response to others' fear [22] is profoundly impaired. These impairments mean that the individual with psychopathy is significantly more difficult to socialize [24]. Interestingly, these impairments, at least when they are indirectly measured by the temperament variable fearfulness, are also associated with weaker conscience development in healthy populations [45].

The vmPFC

The amygdala sends outputs not only to the temporal and visual cortex and regions mediating autonomic responses, but also forward to the vmPFC. Animal studies have produced a relatively precise insight into the functional role of the interaction between the amygdala and the OFC and vmPFC [33]. In particular, Schoenbaum and Roesch implicate the amygdala and vmPFC in stimulus–outcome processing. The basic suggestion is that the amygdala provides reinforcement expectancy information to the OFC and vmPFC; the latter then represents this information. Human neuroimaging work has confirmed the role of the OFC and vmPFC in outcome representation [46].

The individual's 'automatic moral attitude' to a moral transgression thus involves activation of the amygdala by the conditioned stimulus that is the individual's representation of the moral transgression. The amygdala then provides expected reinforcement (both positively and negatively valenced) information, which is represented as a valenced outcome within the vmPFC. Other systems then use this information to select appropriate responses [47]. This information is crucial for reinforcement expectancy-based

Box 3. Treatment

There are successful psychopharmacological and psychotherapeutic programs that reduce aggression associated with many psychiatric conditions [68]. However, currently, psychopathy is regarded as untreatable [67].

Two main lines of data provide interesting potential treatment hypotheses. The first concerns recent work on genetic polymorphisms (Box 2). By understanding the molecular genetics of psychopathy, it should be possible to develop theoretically principled pharmacological treatments. However, this work remains in its infancy. The second and more immediate line is generated by our increased understanding of the pathophysiology of psychopathy; in particular, that it is an emotional disorder associated with reduced activity in the amygdala and associated structures (see main text). This is useful information because there are a variety of known pharmacological agents that modulate amygdala activity. Such agents target, for example, the serotonergic or noradrenergic systems. Much clinical research has focused on the identification of agents that downregulate emotional responding and activity within the amygdala and associated structures. Such agents have been used successfully to treat depression and PTSD, disorders whose primary pathology is increased activity within the amygdala and associated structures [61]. It is possible that the inverse of these treatments might be successfully applied to psychopathy. For example, agents that reduce noradrenergic activity and consequently amygdala activity seem useful in treating PTSD [69]. Perhaps psychopathy could be treated by agents that increase noradrenergic activity?

Although pharmacological agents are likely to be necessary for the successful treatment of psychopathy, they are unlikely to be sufficient. Common treatments for PTSD are designed to reduce emotional responding so that cognitive behavior-based extinction techniques can reduce the emotional significance of the original trauma. Pharmacological agents might be successful in increasing the emotional response and activity within the amygdala and associated structures in individuals with psychopathy. However, such agents will need to be coupled with cognitive behavior-based treatments designed to associate actions that hurt others with an emotional response to the victim's distress.

decision making, including moral reasoning. The disruption in the amygdala and vmPFC in psychopathy means that moral and other forms of reinforcement-based decision making are disrupted [8,48]. Moreover, a recent neuropsychological study demonstrated that vmPFC damage disrupts the avoidance of actions leading to emotionally aversive consequences (e.g. actively killing another person) shown by healthy individuals in moral reasoning paradigms [49]. Interestingly, these systems are recruited in real (virtual) world moral decision making. Both the amygdala and vmPFC show significantly greater activity during appropriate decisions to heal wounded humans or kill attacking monsters than during less appropriate decisions to heal attacking monsters and kill humans [50].

Conclusions

In summary, the model developed here provides a conceptual framework for understanding the functional contribution of the amygdala and vmPFC to the basis of care-based morality and, when dysfunctional, psychopathy. My main argument is that the amygdala enables the forms of learning necessary to care about the welfare of others, and, together with the vmPFC, enables this information to inform moral decision making. However, many questions remain unanswered. Although the functional response described enables an understanding of how the individual might consider an act bad and to be avoided, it does not stipulate the processes necessary to consider that action immoral [17]. Potentially more crucially, it still remains unknown how to translate our increased understanding of the pathophysiology of psychopathy into viable treatment options for individuals with this disorder (Box 3).

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