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The roles of orbital frontal cortex in the modulation of antisocial behavior

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Abstract

This article considers potential roles of orbital frontal cortex in the modulation of antisocial behavior. Two forms of aggression are distinguished: reactive aggression elicited in response to frustration/threat and goal directed, instrumental aggression. It is suggested that orbital frontal cortex is directly involved in the modulation of reactive aggression. It is argued that orbital frontal cortex does not ''inhibit'' reactive aggression but rather may both increase or decrease its probability as a function of social cues present in the environment. Early dysfunction in this function of orbital frontal cortex may be linked to the development of Borderline Personality Disorder. Instrumental aggression is linked to a fundamental failure in moral socialization. However, the available data suggest that the amygdala, but not orbital frontal cortex, is required for functions such as aversive conditioning and passive avoidance learning that are necessary for moral socialization. Psychopathic individuals who present with significant instrumental aggression, are impaired in aversive conditioning and passive avoidance learning and show evidence of amygdala dysfunction. Orbital frontal cortex and the amygdala are involved in response reversal where instrumental responses must be reversed following contingency change. Impairments in response reversal are also seen in psychopathic individuals. However, it remains unclear whether impairment in response reversal per se is associated with antisocial behavior.
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1. Introduction

The level of antisocial behavior in society is a continual source of concern. More than 3 million violent crimes are committed in the US annually (Reiss, Miczek, & Roth, 1994). Twenty thousand of these involve the murder of Americans by gunfire (Sourcebook of Criminal Justice Statistics Online, 1998). There is a growing body of data indicating that there are neurobiological risk factors for antisocial behavior. In this article the role of orbital frontal cortex in the modulation of antisocial behavior will be considered.

It is necessary to first draw a distinction will be drawn between reactive and instrumental aggression (cf. Barratt, Stanford, Dowdy, Liebman, & Kent, 1999; Barratt, Stanford, Kent, & Felthous, 1997; Berkowitz, 1993; Linnoila et al., 1983). In reactive aggression (also referred to as affective aggression), a frustrating or

threatening event triggers the aggressive act and frequently also induces anger. Importantly, the aggression is initiated without regard for any potential goal (for example, gaining the victim's possessions or increasing status within the hierarchy). In contrast, instrumental aggression (also referred to as proactive aggression) is purposeful and goal directed. The aggression is used instrumentally to achieve a specific desired goal (Berkowitz, 1993). This is not usually the pain of the victim but rather the victim's possessions or to increase status within a group hierarchy. Bullying is an example of instrumental aggression and, unsurprisingly, individuals who engage in bullying behaviors, frequently engage in other forms of instrumental antisocial behavior in other contexts (Roland & Idsoe, 2001).

The distinction between reactive and instrumental aggression has been criticized because of some difficulty in characterizing the nature of specific human aggressive episodes (Bushman & Anderson, 2001). However, there is considerable data that there are two relatively

separable populations of aggressive individuals; individuals who present with solely reactive aggression and individuals who present with very high levels of instrumental aggression and also reactive aggression (Barratt et al., 1999; Crick & Dodge, 1996; Linnoila et al., 1983). The potential role of orbital frontal cortex in the modulation of both these forms of aggression will be discussed in turn.

2. Orbital frontal cortex and reactive aggression

In many respects, considerably more is known about reactive than instrumental aggression. This is because a dedicated neural circuitry mediates reactive aggression and humans share this circuitry with other mammalian species (Gregg & Siegel, 2001; Panksepp, 1998). A circuit has been identified that runs from medial amygdaloidal areas downward, largely via the stria terminalis to the medial hypothalamus, and from there to the dorsal half of the periaqueductal gray (PAG). The system is organized in a hierarchical manner such that aggression evoked from the amygdala is dependent on functional integrity of the medial hypothalamus and PAG but that aggression evoked from the PAG is not dependent on the functional integrity of the amygdala (Bandler, 1988; Gregg & Siegel, 2001; Panksepp, 1998). This circuitry mediates the animal's response to threat. At low levels of stimulation, from a distant threat, the animal will freeze. At higher levels, from a closer threat, the animal will attempt to escape the environment. At higher levels still, when the threat is very close and escape is impossible, the animal will display reactive aggression (Blanchard, Blanchard, & Takahashi, 1977).

Both the amygdala and orbital frontal cortex modulate the neural circuitry mediating reactive aggression though their roles differ. The amygdala is known to react to reinforcing as well as aversive stimuli (Everitt, Cardinal, Hall, Parkinson, & Robbins, 2000). This suggests that the amygdala would be in a position to both upgrade (as a response to an aversive stimulus) or downgrade (as a response to reinforcement) the responsiveness of the sub-cortical systems that respond to threat. Indeed, this is suggested by the augmentation of the startle reflex literature. The startle reflex is mediated by the sub-cortical systems that respond to threat. It can be modulated by the presence of visual or auditory primes that occur shortly before the startle stimulus. Aversive visual threat primes augment the magnitude of the startle reflex relative to neutral primes while appetitive visual primes reduce the magnitude of the startle reflex (Lang, Bradley, & Cuthbert, 1990). This modulation is achieved by the operation of the amygdala on the sub-cortical systems responding to threat that generate the reflex (Angrilli et al., 1996; Campeau & Davis, 1995; Davis, 2000; Funayama, Grillon, Davis, & Phelps, 2001). Given the

ability of the amygdala to upgrade or downgrade the responsiveness of the sub-cortical systems that respond to threat as indicated by the startle reflex literature, amygdala lesions might therefore reduce the probability of reactive aggression in threatening circumstances by reducing the patient's sensitivity to learned threat. Learned threats would not activate the amygdala and through the amygdala, the sub-cortical system mediating reactive aggression. However, amygdala lesions might also increase the probability of reactive aggression in non-threatening circumstances. The amygdala lesion would prevent the suppression of reactive aggression as a function of amygdala activation by appetitive stimuli in the environment. This suggests that amygdala lesions might either increase or decrease the probability of reactive aggression depending on the contextual parameters the animal is exposed to. The literature certainly indicates that amygdala lesions can both increase or decrease the probability of reactive aggression. Thus, bilateral amygdalectomies have been reported to decrease aggressive behavior in 70–76% of cases (Ramamurthi, 1988). However, very severe amygdalar atrophy is found in a significant subgroup of aggressive patients with temporal lobe epilepsy (van Elst, Woermann, Lemieux, Thompson, & Trimble, 2000). Moreover, unilateral damage to the central nucleus of the amygdala in cats increases the expression of reactive aggression (Zagrodzka, Hedberg, Mann, & Morrison, 1998).

Both the animal, and human neuro-psychological literature, suggest that frontal cortex is involved in the modulation of the sub-cortical circuit mediating reactive aggression (Anderson, Bechara, Damasio, Tranel, & Damasio, 1999; Grafman, Schwab, Warden, Pridgen, & Brown, 1996; Gregg & Siegel, 2001; Panksepp, 1998; Pennington & Bennetto, 1993). Certainly, damage to medial frontal and orbital frontal cortex is associated with increased risk for the display of reactive aggression in humans whether the lesion occurs in childhood (Anderson et al., 1999; Pennington & Bennetto, 1993) or adulthood (Grafman et al., 1996). In addition, there are considerable neuro-imaging data assessing the neural functioning of patients with reactive aggression. These data have revealed reduced frontal functioning in patients presenting with reactive aggression (Soderstrom, Tullberg, Wikkelso, Ekholm, & Forsman, 2000; Volkow & Tancredi, 1987; Volkow et al., 1995). Interestingly, this reduced frontal functioning is not observed in patients presenting with predominantly instrumental aggression (Raine et al., 1998). This is consistent with neuro-psychological data that indicate that psychopathic individuals, individuals who present with marked instrumental aggression, do not present with poor performance on general measures of frontal lobe functioning (Kandel & Freed, 1989; LaPierre, Braun, & Hodgins, 1995; Mitchell, Colledge, Leonard, & Blair, 2002).

Unfortunately, however, the above studies have placed little emphasis on considering the separable regions of frontal cortex. This is despite the fact that the neuro-psychological data strongly suggest that only medial and orbital frontal cortex are involved in modulating reactive aggression; dorsolateral prefrontal cortex appears to have little role (Grafman et al., 1996). However, one of the few studies to dissociate functional regions of frontal cortex with regard to aggression was conducted by Goyer and colleagues who examined the CBF under rest conditions using PET of 17 patients with personality disorder (antisocial, borderline, dependent, and narcissistic) and 43 comparison individuals (Goyer et al., 1994). The patients' aggression was predominantly reactive. They found that it was lower normalized CBF in lateral orbital frontal cortex (BA 47) that correlated with a history of reactive aggression.

Orbital frontal cortex is involved in at least two processes that modulate the sub-cortical systems mediating reactive aggression. The first is the computation of expectations of reward and identifying if these expectations have been violated (Rolls, 2000). 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. Orbital frontal cortex is involved in the expectation violation computations necessary to induce frustration. It can therefore be suggested that orbital frontal cortex may increase neuronal activity in the sub-cortical systems mediating reactive aggression under conditions when an expected reward has not been achieved and suppress neuronal activity when the expected reward is achieved.

The second process is Social Response Reversal (SRR: Blair & Cipolotti, 2000). It has been suggested that regions of orbital frontal cortex are involved in a system that is crucial for social cognition and the modulation of reactive aggression (Blair & Cipolotti, 2000). The position stresses the role of social cues in modulating social behavior (Blair, 2001; Blair & Cipolotti, 2000). Thus, angry expressions are known to curtail the behavior of others in situations where social rules or expectations have been violated (Averill, 1982).

The SRR system is thought to be activated by several classes of stimuli: (1) another individual's angry expressions; (2) other negative valence expressions (e.g., staring that can precede a sense of embarrassment and perhaps others' disgusted expressions); and (3) situations associated with social disapproval. Certainly, orbitofrontal cortex (Brodmann's Area 47) is activated by negative emotional expressions; in particular, anger but also fear and disgust (Blair, Morris, Frith, Perrett, & Dolan, 1999; Kesler/West et al., 2001; Sprengelmeyer, Rausch, Eysel, & Przuntek, 1998). Moreover, patients with orbital frontal cortex lesions are impaired in the ability to recognize facial expressions, particularly anger

(Blair & Cipolotti, 2000; Hornak, Rolls, & Wade, 1996). Such patients have also been found to show impairment in appropriately attributing anger and embarrassment to story protagonists (Blair & Cipolotti, 2000). In addition, such patients have a deficit in identifying the sorts of violations of social norms that induce anger in others (Blair & Cipolotti, 2000; Stone, Baron-Cohen, & Knight, 1998). Importantly, recent neuro-imaging data have shown that the same region of lateral orbitofrontal cortex (BA 47) that responds to angry expressions also responds to social norm violations; situations likely to induce social disapproval (anger) in others (Berthoz, Armony, Blair, & Dolan, 2002).

The suggestion is that the SRR system modulates current behavioral responding, in particular the modulation of reactive aggression. Importantly, it is suggested that the form of modulation is a function of the displaying animal's position in the dominance hierarchy. Thus, for example, the angry expression of an individual higher in the dominance hierarchy will suppress reactive aggression and lead to alterations in current instrumental behavior. In contrast, the angry expression of an individual lower in the dominance hierarchy will lead to activation of the sub-cortical circuitry for reactive aggression. In line with this, there are data from work with primates demonstrating that reactive aggression is modulated by the individual's position in the dominance hierarchy. Thus, neurally stimulated animals will vent their rage on more submissive animals and avoid confrontations with more dominant ones (Alexander & Perachio, 1973).

The SRR system is thought to be dissociable from the system, also recruiting regions of orbital frontal cortex, that computes violations of reward expectancies (Blair & Cipolotti, 2000). Indeed, a double dissociation has been observed in psychopharmacological work. Thus, GABAergic compounds such as alcohol and diazepam impair social response reversal (Blair & Curran, 1999; Borrill, Rosen, & Summerfield, 1987; Zangara, Blair, & Curran, 2002) but not response reversal to contingency change (Coull, Middleton, Robbins, & Sahakian, 1995). In contrast, serotonergic manipulations modulate response reversal to contingency change (Murphy, Smith, Cowen, Robbins, & Sahakian, 2002; Park et al., 1994; Rogers et al., 1999) but not social response reversal (Harmer, Bhagwagar, Cowen, & Goodwin, 2001). Such double dissociation data can be taken to indicate that the dissociated systems can be thought of as functionally separable (Shallice, 1988).

The model developed here is depicted in Fig. 1. Reactive aggression is mediated by medial amygdaloid areas, the medial hypothalamus, and the dorsal half of the PAG (Gregg & Siegel, 2001; Panksepp, 1998). The amygdala and lateral orbital frontal cortex (BA 47), modulate this circuit. The modulation by the amygdala occurs as a function of the presence of threat or appe-
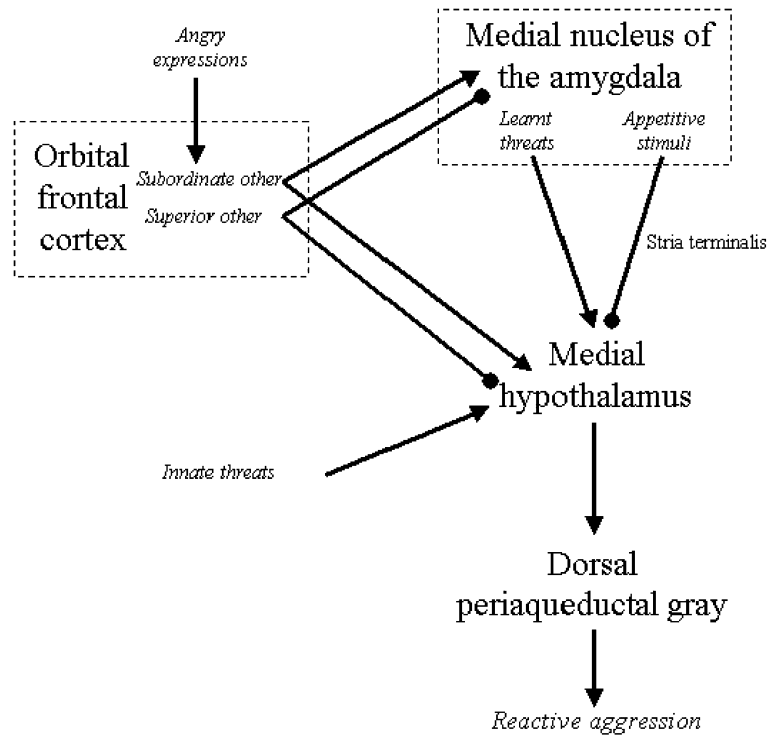
Fig. 1. Systems involved in reactive aggression and their putative roles: reactive aggression is mediated by medial amygdaloid areas, the medial hypothalamus, and the dorsal half of the periaqueductal gray (Gregg & Siegel, 2001; Panksepp, 1998). The amygdala modulates these systems as a function of the presence of threat or appetitive cues in the environment. Orbital frontal cortex modulates these systems as a function of social emotional cues and knowledge of the position of con-specifics in the current dominance hierarchy.

titive cues in the environment. The modulation by frontal cortex occurs as a function of social emotional cues, representations of cultural norms and knowledge of the other individuals' position in the dominance hierarchy.

Much of the data presented above is obtained from work with neurological patients, individuals who have been described as presenting with "pseudo-psychopathy" (Blumer & Benson, 1975) or "acquired sociopathy" (Damasio, 1994). However, there do appear to be developmental forms of these neurological syndromes. These developmental forms are likely to be linked to either genetic or early environmental influences. It will be argued below that psychopathy is not one of these developmental forms; psychopathic individuals show profound levels of instrumental antisocial behavior, completely unlike patients with orbital frontal cortex lesions (Cornell et al., 1996; Williamson, Hare, & Wong, 1987). Patients with Borderline Personality Disorder (BPD), in contrast, presents very similarly to patients with orbital frontal cortex lesions. Patients with BPD are characterized by impulsive aggressive behaviors, affective instability, inappropriate intense anger, and unstable interpersonal relationships (Association, 1994). In addition, a similar population with what has been termed Intermittent Explosive Disorder (IED) have been characterized; these are individuals who present with a chronic pattern of aggression that is out of proportion to the provocation (Coccaro, 1998). Patients with BPD and IED appear to have generalized orbital frontal cortex dysfunction with both response reversal to contingency change and social response reversal affected. The functioning of both patients with BPD and IED is characterized by impairment on classic response reversal measures of orbital frontal cortex functioning (Best, Williams, & Coccaro, 2002; Leyton et al., 2001). Moreover, both populations show general expression recognition difficulties with notable problems with angry expressions (Best et al., 2002). Finally, two neuro-imaging studies have identified atypical responding in lateral orbital frontal cortex (BA 47) in patients with BPD (Goyer et al., 1994; Herpertz et al., 2001).

3. Orbital frontal cortex and instrumental aggression

Instrumental aggression is goal directed motor activity and, as such, is likely to recruit the same cortical neural systems as any other goal directed motor program. In brief, these neural systems would include temporal cortex, to represent the object, and striatal and premotor cortical neurons to implement the actual behavior (Passingham & Toni, 2001). It is unlikely that elevated levels of instrumental behavior in specific in-

dividuals are due to abnormalities in any of the systems for motor behavior; individuals presenting with heightened levels of instrumental aggression do not show general motor impairment. Instead, it is likely that such individuals show elevated levels of instrumental behavior because they have been reinforced, and not punished, for committing such behavior in the past.

Moral socialization is the term given to the process by which care-givers, and others, reinforce behaviors that they wish to encourage and punish behaviors that they wish to discourage. Importantly, the unconditioned stimulus (US; the punisher) that best achieves moral socialization as regards instrumental antisocial behavior is the victim of the transgression's pain and distress; empathy induction, focusing the transgressor's attention on the victim, particularly fosters moral socialization (Eisenberg, 2002; Hoffman, 1994). Moral socialization involves aversive conditioning and instrumental learning (Eysenck, 1964; Fowles, 1988; Fowles & Kochanska, 2000; Trasler, 1973). Thus, in order to learn that hitting another is bad, a representation of this action must be associated with an aversive unconditioned stimulus (e.g., the distress of the victim) through aversive conditioning. Similarly, learning to avoid committing moral transgressions involves either personally committing, or viewing another commit, a moral transgression and then being 'punished' by the aversive response of the victim's distress; in other words it involves instrumental conditioning/passive avoidance learning (Blair, 1995).[1]

The amygdala is crucially implicated in aversive conditioning and instrumental learning (Davis, 2000; Killcross, Robbins, & Everitt, 1997; LeDoux, 1998). This has been shown through work with animals and humans with neurological lesions (Bechara et al., 1995; LaBar, LeDoux, Spencer, & Phelps, 1995). The amygdala enables representations of conditioned stimuli to elicit conditioned responses through the brainstem (during aversive conditioning) and representations of conditioned stimuli to be associated with specific responses for rewards (during instrumental learning). Moreover, the amygdala is implicated in a particular form of instrumental learning, passive avoidance learning, where the individual must withhold from responding to particular stimuli that, if responded to, result in punishment (Ambrogi Lorenzini, Baldi, Bucherelli, Sacchetti, & Tassoni, 1999).[2]

The data thus suggest that the cause of an individual's elevated levels of instrumental aggression is likely to be related to a breakdown in moral socialization; either there has been a lack of the formative learning experiences or the neuro-cognitive architecture mediating moral socialization is dysfunctional. As mentioned above, psychopathy is a developmental disorder marked by highly elevated levels of instrumental antisocial behavior (Cornell et al., 1996; Williamson et al., 1987). In childhood and adolescence, psychopathic tendencies are identified principally by either the use of the Antisocial Process Screening Device (Frick & Hare, 2001) or by the Psychopathy Checklist: Youth Version (Forth, Kosson, & Hare, in press; Kosson, Cyterski, Steuerwald, Neumann, & Walker-Matthews, 2002). In adulthood, psychopathy is identified though use of the Psychopathy Checklist-Revised [PCL-R] (Hare, 1991). Psychopathic individuals notably also present with a characteristic pattern of emotional impairment: reduced anxiety, empathy for their victims and guilt (Cleckley, 1967; Frick, Lilienfeld, Ellis, Loney, & Silverthorn, 1999; Hare, 1991). The suggestion is that psychopathy is related to a breakdown in moral socialization; the affective systems that mediate aversive and instrumental conditioning as a response to another's sadness and fear are dysfunctional (Blair, 1995; Blair, Jones, Clark, & Smith, 1997). At the neural level, the claim is that that this is due to amygdala dysfunction (Blair, 2001; Blair et al., 1999; Patrick, 1994).

There are now considerable data in support of these claims. Thus, a recent volumetric magnetic resonance imaging (MRI) study has found a highly significant negative correlation between level of psychopathy and amygdala volume (Tiihonen et al., 2000). Moreover, a functional MRI study investigating neural responses to words of neutral and negative valence found a reduced amygdala response in the high PCL-R scoring group relative to the low PCL-R scoring group during the processing of words of negative valence. There was no such group difference for the neutral words (Kiehl et al.,

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[1] Here the emphasis is placed on aversive stimuli processing in socialization. However, there have been suggestions that socialization can alternatively capitalize on appetitive processing (Maccoby, 1983). Individuals with psychopathy present with relatively intact appetitive processing, at least relative to their pronounced difficulties with aversive processing (Blair et al., inpress; Peschardt, Morton, & Blair, 2003). This suggests that the development of instrumental aggression showy by individuals with psychopathy might require a lack of affectively positive parent–child interaction as well as temperamental hypo-responsivity in the child (Fowles & Kochanska, 2000).

[2] It is important here to distinguish between passive avoidance learning, response reversal learning, and extinction. Passive avoidance learning involves the participant learning to avoid responding to a particular *novel* stimulus. In contrast, response reversal learning involves learning to avoid responding to a *familiar* stimulus that, when responded to previously, had resulted in reward but now results in punishment in favor of responding to another *familiar* stimulus that, when responded to previously, had resulted in punishment but now results in reward. Response reversal is involved in the response reversal component of the ID/ED task (Dias, Robbins, & Roberts, 1996). Extinction involves the cessation of a response to a *familiar* stimulus when reward ceases to be forthcoming. Newman's card playing task is an example of an extinction task (Newman, Patterson, & Kosson, 1987).

2001). Functionally, psychopathic individuals are impaired on tasks known to rely on the functioning of the amygdala. They thus show impaired aversive conditioning (Lykken, 1957) and reduced augmentation of the startle reflex by threat primes (Levenston, Patrick, Bradley, & Lang, 2000). They also show impaired passive avoidance learning (Newman & Kosson, 1986) and instrumental learning (Fine et al., submitted). As regards processing the distress of other individuals, psychopathic individuals have been found to show reduced autonomic activity to other's sadness (Aniskiewicz, 1979; Blair et al., 1997; House & Milligan, 1976) and reduced recognition of the fearful expressions of others (Blair, Colledge, Murray, & Mitchell, 2001).

There have been reports that neurons in orbital frontal cortex respond differentially to stimuli during aversive conditioning and instrumental and passive avoidance learning (Garcia, Vouimba, Baudry, & Thompson, 1999; Schoenbaum, Chiba, & Gallagher, 1999; Tremblay & Schultz, 1999). However, lesions of orbital frontal cortex do not impair aversive conditioning (Quirk, Russo, Barron, & Lebron, 2000) or instrumental learning/passive avoidance (Schoenbaum, Nugent, Saddoris, & Setlow, 2002); in short, orbital frontal cortex, unlike the amygdala, is not necessary for either function.

The orbital frontal cortex (and the amygdala) is necessary for appropriate behavioral change following reinforcer devaluation (Baxter, Parker, Lindner, Izquierdo, & Murray, 2000; Gallagher, McMahan, &

Schoenbaum, 1999). In addition, orbital frontal cortex is crucial for response reversal and extinction. In short, it is necessary for changing a response to a stimulus when the reinforcement contingencies change (Dias et al., 1996; Rolls, Hornak, Wade, & McGrath, 1994). Moreover, orbital frontal cortex has been linked to decision making when knowledge about potential positive and negative results is necessary to guide behavioral responding (e.g., Bechara, Damasio, Damasio, & Anderson, 1994; Rogers et al., 1999); though, for data challenging the role of orbital frontal cortex, per se, in these tasks, see (Manes et al., 2002).

3.1. A model of the role of orbital frontal cortex in response selection

A preliminary model of the role of orbital frontal cortex in guiding behavioral responding is developed in Fig. 2. The model supposes a commonality of function of orbital frontal cortex with other regions of frontal cortex. There have been several recent suggestions that left dorsolateral prefrontal cortex, in particular, is involved in the selection of a response option when more than one is in competition (Frith, 2000; Robinson, Blair, & Cipolotti, 1998). These have been elegantly modeled computationally (Usher & Cohen, 1999). Very briefly, the Usher and Cohen (1999) model assumes the existence of modality specific posterior units that are limited by temporal decay while anterior units use active reverberations that can sustain themselves and that are
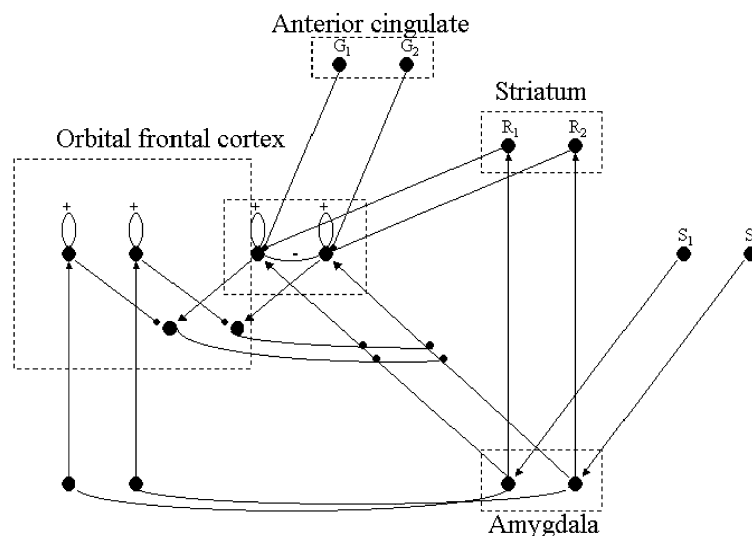

Fig. 2. Model of the role of orbital frontal cortex in guiding behavioral responding: Units in orbital frontal cortex are crucial for the selection of a response when stimuli (e.g., S_1 and S_2) activate multiple competing responses (R_1 and R_2). Response competition is rapidly resolved as the anterior units are self excitatory but mutually inhibitory (cf. Usher & Cohen, 1999). These orbital frontal cortex units resolve response competition as a function of the initial activation states of the basal ganglia units, expectations of reinforcement from amygdala units and units, possibly in anterior cingulate, representing desired goal states. Comparator units detect mismatches between expectations of reinforcement and actual reinforcement. When activated these disrupt the connections (weights) between amygdala units and orbital frontal cortex units as a function of the degree of the previous strength of these connection weights. This disruption allows another unit to develop the new expectation of reinforcement associated with the changed contingency to the stimulus and thus ease response change.

limited by displacement from competing new information. The anterior units by being self excitatory but mutually inhibitory allow rapid selection between competing, multiply active posterior response options (Usher & Cohen, 1999). The suggestion here is that units in orbital frontal cortex may serve a similar function over units in basal ganglia that mediate motor responses (see Fig. 2). The units in orbital frontal cortex would receive information in order to solve response competition on the basis of not only the activation of basal ganglia units but also expectations of reinforcement provided by the amygdala. In addition, they would receive input from units, possibly in anterior cingulate, representing desired goal states. The suggestion would be that reinforcer devaluation (Baxter et al., 2000; Gallagher et al., 1999) would reduce potential activation of the corresponding units in orbital frontal cortex. This would reduce the probability that a response associated with these units would be chosen; the units involved would be less likely to win out in competition with other units that had not associated with reinforcer devaluation. Within this model, comparator units would detect mismatches between expectations of reinforcement and actual reinforcement. When activated these would disrupt the connections (weights) between amygdala units and orbital frontal cortex units (connections from 3 to 2) as a function of the degree of the previous strength of these connection weights. Thus, under conditions where reinforcement had been a certainty and the connection weights were high, there would be considerable disruption while if the reinforcement contingency was less obvious and the connection weights were lower, there would be less disruption. This disruption process would allow another unit to develop the new expectation of reinforcement associated with the changed contingency to the stimulus and thus ease response change.

Within the model, as the data suggest (e.g., Schoenbaum et al., 2002), orbital frontal cortex is not seen as necessary for instrumental learning and passive avoidance learning. However, the known role of orbital frontal cortex in response reversal (Dias et al., 1996; Rolls et al., 1994) is seen as a function of the degree to which there is a mismatch between the expectation of reinforcement, provided by the amygdala to orbital frontal cortex, and the presence of reinforcement. This suggests that if there is dysfunction in either the amygdala, orbital frontal cortex or the connections between the amygdala and orbital frontal cortex, response reversal will be detrimentally affected. Moreover, the greater the degree of dysfunction, the more difficult it will be for the individual to identify the contingency change.

Children with psychopathic tendencies and adult psychopathic individuals show comparably impaired performance on measures of amygdala functioning such as passive avoidance (Newman & Kosson, 1986; New-

man, Widom, & Nathan, 1985), the processing of fearful expressions (Blair, Colledge, & Mitchell, 2001) and aversive conditioning (Lykken, 1957; Raine, Venables, & Williams, 1996). However, there is less clear evidence that children with psychopathic tendencies show comparably impaired performance on measures requiring orbital frontal cortex such as extinction or response reversal tasks. Newman's card playing task (Newman et al., 1987) involves extinction; the participant learns to play the card for reward but then must extinguish this response as, proceeding through the pack of cards, the probability of reward decreases successively. Both children with psychopathic tendencies and adult psychopathic individuals do show marked impairment on this task (Fisher & Blair, 1998; Newman et al., 1987; O'Brien & Frick, 1996). However, the ID-ED paradigm also includes response reversal; the participant must reverse their responding from the object that, when responded to, had elicited reward but that now elicits punishment. While adult psychopathic individuals show notable impairment in response reversal on this task (Mitchell et al., 2002), children with psychopathic tendencies do not (Blair et al., 2001). A major difference between these two tasks is in the salience of the contingency change. In the card playing task, the probability of reinforcement decreases by 10% over every 10 trials. In the ID-ED task, the probability of reinforcement changes from 100 to 0% once the initial learning criteria has been achieved. This indicates that while both children with psychopathic tendencies and adult psychopathic individuals are impaired in the detection of contingency change, this impairment is markedly greater in the adult psychopathic individuals. Moreover, this suggests that if we reduce the salience of the contingency change, we should see impairment in the children with psychopathic tendencies and that the degree of impairment will be a function of the salience of the contingency change. This was tested using a probabilistic response reversal paradigm. Participants were presented with pairs of stimuli. For each pair, one of the stimuli was rewarded more often than the other. The probability of reward was different across pairs (for pair 1, stimulus 1 was rewarded 100% of the time, for pair 2, stimulus 3 was rewarded 90% of the time, etc.). Following a set number of trials the contingency was reversed (for pair 1, stimulus 2 was rewarded 100% of the time, for pair 2, stimulus 4 was rewarded 90% of the time). While the children with psychopathic tendencies showed no difficulty reversing their responses for salient contingency changes, they did show significant difficulty as the salience of the contingency change decreased (Budhani et al., in preparation).

The data therefore suggest that adults with psychopathy present with markedly more pronounced orbital frontal cortex impairment than children with psychopathy tendencies. This suggests two possibilities:

first, that the children with psychopathic tendencies are a less affected population than the adults with psychopathy. In other words, the full presentation of adult psychopathy is a result of both amygdala and orbital frontal cortex dysfunction. This possibility cannot be dismissed. However, it is important to note that the children with psychopathic tendencies present with severe emotional disturbance (they show reduced guilt and a lack of a significant attachments) (Frick & Hare, 2001; Frick, O'Brien, Wootton, & McBurnett, 1994). This then suggests that the emotional disturbance is related to the amygdala dysfunction even if the full presentation of the disorder, seen in the adults, also requires orbital frontal cortex dysfunction.

A second possibility is that we are beginning to document the developmental course of the disorder. It is possible that psychopathy is marked by amygdala dysfunction in childhood but that by adulthood related structures are also affected. The amygdala and orbital frontal cortex are massively interconnected (Amaral, Price, Pitkanen, & Carmichael, 1992; Rolls, 1997). It is possible that due to the interconnections of the amygdala and orbitofrontal cortex, a reduction in afferent input from the amygdala (because of the primary amygdala dysfunction) may, over time, have a negative impact on the responsiveness of the orbitofrontal cortex. We therefore may see reduced sensitivity to contingency change in individuals with psychopathy as they age. Alternatively, the greater orbitofrontal cortex dysfunction seen in the adults is a secondary consequence of some of the behavioral characteristics of psychopathy. For example, one of the criteria of psychopathy, stimulation seeking, is often associated with drug use (Hare, 1991). Studies suggest that psychopathy is associated with higher rates of drug abuse, and multiple drug use (Hemphill, Hart, & Hare, 1994; Smith & Newman, 1990). Using a novel decision-making task, Rogers et al. (1999) assessed the quality of decision-making and deliberation time of individuals with focal orbitofrontal cortex damage, and individuals who abused amphetamine or opiates. All three groups showed impaired performance on the task relative to comparison groups. Furthermore, chronic amphetamine abusers showed a pattern of sub-optimal decision-making that correlated with their years of abuse (Rogers et al., 1999). Given the neuro-cognitive impairments associated with chronic drug abuse, and the data suggesting higher rates of abuse and dependence among psychopathic individuals, we cannot discount the possibility that some of the decision-making impairments seen in psychopathic individuals are acquired as a secondary consequence of the stimulus seeking behavior characteristic of the disorder.

In conclusion, the orbital frontal cortex, unlike the amygdala, does not appear to be crucial for processes such as aversive conditioning, instrumental learning and passive avoidance that are crucial for moral socializa-

tion. Indeed, it remains at present unclear whether orbital frontal cortex dysfunction does increase risk for instrumental, rather than reactive, aggression. Orbital frontal cortex, in conjunction with the amygdala, is involved in response reversal. Children with psychopathic tendencies and particularly adult psychopathic individuals, do show impairment in response reversal. However, it is by no means obvious why difficulties in response reversal are likely to increase the probability of instrumental aggression. Of course, it is possible that these difficulties with response reversal might be related to increased frustration based, reactive aggression that is also seen in individuals with psychopathy.

4. General conclusion

In conclusion, it is important to distinguish between reactive and instrumental aggression. These forms of aggression are associated with different developmental disorders. Patients with Borderline Personality Disorder present with reactive aggression. Psychopathic individuals present with marked levels of instrumental aggression as well as reactive aggression.

Orbital frontal cortex is involved in the modulation of reactive aggression. It does not "inhibit" reactive aggression but rather may both increase or decrease its probability as a function of social cues present in the environment. Orbital frontal cortex is less obviously involved in the modulation of instrumental aggression. Orbital frontal cortex is not necessary for those functions such as aversive conditioning and passive avoidance learning that are necessary for moral socialization. However, orbital frontal cortex is involved in response reversal. Impairments in response reversal are seen in psychopathic individuals. However, it remains unclear whether impairment in response reversal is associated with antisocial behavior.

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