JOURNAL OF CHILD AND ADOLESCENT PSYCHOPHARMACOLOGY
Volume 26, Number 1, 2016

Pp. 4–9
DOI: 10.1089/cap.2015.0088

**Original Articles**

# The Neurobiology of Impulsive Aggression

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## Abstract

This selective review provides a model of the neurobiology of impulsive aggression from a cognitive neuroscience perspective. It is argued that prototypical cases of impulsive aggression, those associated with anger, involve the recruitment of the acute threat response system structures; that is, the amygdala, hypothalamus, and periaqueductal gray. It is argued that whether the recruitment of these structures results in impulsive aggression or not reflects the functional roles of ventromedial frontal cortex and dorsomedial frontal and anterior insula cortex in response selection. It is also argued that impulsive aggression may occur because of impaired decision making. The aggression may not be accompanied by anger, but it will reflect disrupted evaluation of the rewards/benefits of the action.

## Introduction

Aggression can be defined as behavior directed toward harming or injuring another living being who is motivated to avoid such treatment. It is a natural and adaptive part of the mammalian social behavioral repertoire. However, it can become maladaptive if it is exaggerated, persistent, or expressed out of context (Connor et al. 2006; Nelson and Trainor 2007). Aggressive and antisocial behaviors are the leading cause of all child and adolescent referrals to mental health clinicians (Berkowitz 1993). Each antisocial individual has been calculated to cost society up to 10 times more than their healthy counterparts in aggregate healthcare and social service expenditures (Nelson and Trainor 2007). Aggression, therefore, is a serious social concern and is an economic burden on society.

Impulsive, also known as reactive, aggression is contrasted with planned or instrumental aggression (Berkowitz 1993; Dodge et al. 1997). Instrumental aggression is goal directed (e.g., mugging for the purpose of stealing someone's wallet), whereas impulsive (reactive) aggression is initiated as a response to a provocation, without any identifiable goal (Blair 2010).

The ability to classify individual aggressive acts as impulsive or instrumental has been questioned however (Bushman and Anderson 2001). An example of this would be attempting to classify an incident involving someone shooting a person 5 days after discovering that that person had been having an affair with the shooter's spouse. There is a clear reactive component (anger and frustration); however, the action is planned and, as a gun is used, definitively instrumental. However a distinction can be made between the neural systems that mediate impulsive/reactive aggression to an intense threat and those involved in choosing among instrumental acts, including instrumental aggression. These neural systems will be considered. In addition, it will be argued that the systems involved in response choice also influence whether impulsive aggression is expressed.

It will be argued that: 1) There is a neural circuit that mediates the acute threat response (amygdala, hypothalamus, periaqueductal gray [PAG]) which, when activated to a sufficient degree, initiates impulsive aggression; 2) as a function of its role in representing action values and response choice, the ventromedial frontal cortex (vmPFC) partially determines whether acute threat systems activation results in impulsive aggression; and 3) vmPFC is implicated in reinforcement-based decision making. If vmPFC functioning is compromised, reinforcement-based decision making will be disrupted, leading to ''impulsive'' behavior including ''impulsive'' aggression. A fourth argument that will be made is that the dorsomedial frontal and anterior insula cortices are also involved in reinforcement-based decision making and also influence, together with vmPFC, whether impulsive aggression is expressed (see Fig. 1).

## The Acute Threat Response

Animals demonstrate a gradated and instinctual response to threat. Distant threats induce freezing, then, as they draw closer, flight, and, finally, impulsive aggression when they are very close and escape is impossible (Blanchard et al. 1977). As such, impulsive aggression can involve unplanned, enraged attacks on the object perceived to be the threat source. Animal studies have indicated that impulsive aggression is mediated via a circuit that runs from the medial amygdala, largely via the stria terminalis to the medial hypothalamus and from there to the dorsal half of the PAG (Panksepp 1998; Gregg and Siegel 2001; Nelson and Trainor 2007; Lin et al. 2011). It has been argued that this circuit mediates impulsive aggression in humans also, not only to threat but also to

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**Funding:** This work was supported by the Intramural Research Program of the National Institute of Mental Health, National Institutes of Health under grant number 1-ZIA-MH002860-08.

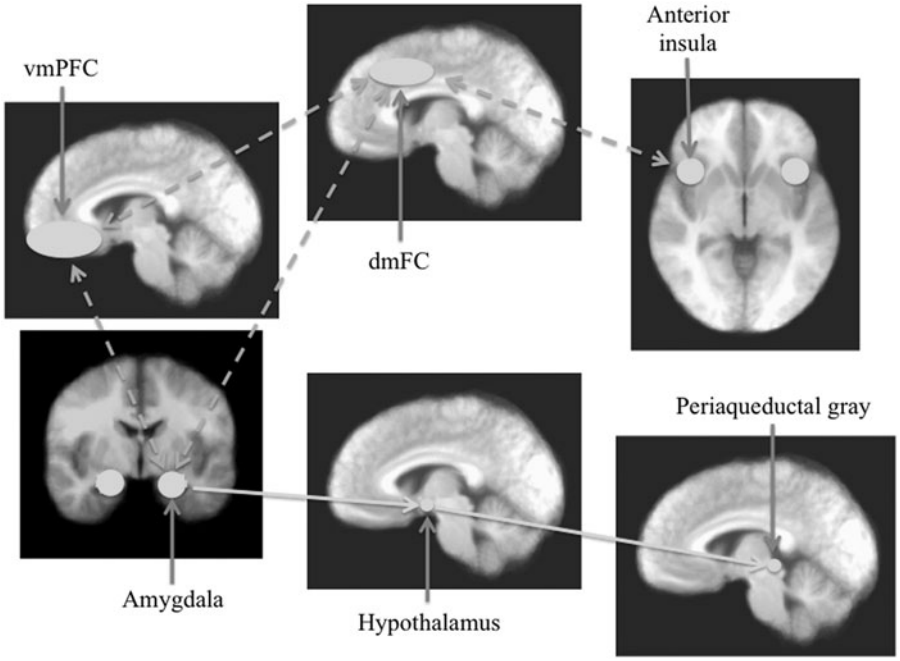


**FIG. 1.** Systems implicated in impulsive aggression. The circuit running from the amygdala to the hypothalamus and from there to the periaqueductal gray is thought to mediate reactive aggression. The probability that activation of this circuit is expressed as reactive aggression is partly determined by systems implicated in reinforcement-based decision making including the ventromedial (vmPFC) and dorsomedial frontal (dmFC) and anterior insula cortices (AIC). The vmPFC is particularly important for representing the value of actions and objects. The dmFC is thought to use this value information to affect response choice (Hare, Camerer, Rangel, 2009), partly implemented through the AIC.

frustration and social provocation ( Blair 2004). Three strands of data support this argument.

First, functional magnetic resonance imaging (fMRI) work with humans has shown that the increasing proximity of a threat is associated with increased activity within the amygdala, hypothalamus and PAG (Mobbs et al. 2007, 2009, 2010; Coker-Appiah et al. 2013). In addition, recent work has demonstrated that these regions also respond to frustrating stimuli. In this study, participants were blocked from obtaining a reward with levels of experienced frustration being parametrically varied by manipulating the participants' motivation to obtain the reward prior to blocking (Yu et al. 2014).

Second, there has been work with laboratory-based ''models'' of impulsive aggression: The Taylor Aggression Paradigm (TAP) (Taylor 1967), the Point Subtraction Aggression Paradigm (PSAP) (Cherek et al. 1997), and computationally similar social exchange paradigms (Strobel et al. 2011; White et al. 2013a, 2014a). In these tasks, participants have the opportunity to retaliate to other individuals' actions (e.g., previous punishments [TAP], point removals [PSAP], or unfair allocations [social exchange]). In all cases, the participants' aggressive responses (retaliatory responses) are a function of provocation level (Cherek et al. 1997; White et al. 2014a).

Before continuing, it is worth noting that whereas the TAP and PSAP (and retaliatory versions of social exchange) paradigms are considered to index impulsive aggression (Taylor 1967; Cherek et al. 1997), they do not *simply* index impulsive aggression. Unfair provocations initiate anger, a definitional feature of impulsive aggression (Berkowitz 1993; Cherek et al. 1997; Sanfey et al. 2003). However, they do not only elicit an instinctual response to threat or intruders. Rather, the participant plans a response, choosing how much to retaliate to the other individual (Cherek et al. 1997; White et al. 2014a). As such, retaliatory behavior should involve activity within acute threat response systems and regions involved in response choice/decision making (discussed subsequently).

In line with the idea that impulsive retaliation will be associated with increased acute threat response system activity, retaliation on the TAP and in social exchange paradigms elicits activity within the amygdala, hypothalamus, and PAG. For example, high relative to low punishments to the competitor on the PSAP have been associated with increased activity within the amygdala and hypothalamus (extending proximal to the PAG) (Veit et al. 2010). Similarly, decisions to reject the proposer's unfair offers on social exchange paradigms are associated with increased activity within the PAG (Sanfey et al. 2003; Tabibnia et al. 2008; Corradi-Dell' Acqua et al. 2013). Moreover, the level of punishment delivered to an unfair partner is directly related to the level of PAG activity (Strobel et al. 2011; White et al. 2013a, 2014b).

The third strand of data supporting the argument that the acute threat response systems (amygdala, hypothalamus, and PAG) mediate impulsive aggression comes from work with patient populations at increased risk for impulsive aggression. Given the literature briefly reviewed previously, it can be predicted that such patients will show heightened responsiveness in regions implicated in impulsive aggression to emotional provocation (Blair 2001) ; that is, the amygdala, hypothalamus, and PAG (Panksepp 1998; Gregg and Siegel 2001; Nelson and Trainor 2007; Lin et al. 2011). In line with this suggestion, patients with posttraumatic stress disorder (PTSD) (Shin et al. 2006), intermittent explosive disorder (Coccaro et al. 2007), severe mood dysregulation (Thomas et al. 2013), and borderline personality disorder (Hazlett et al. 2012), as well as impulsively aggressive spouse abusers (Lee et al. 2008), all with an increased risk for reactive aggression, all show increased amygdala responsiveness to threatening stimuli relative to comparison

individuals. Moreover, a recent study reported a positive association between propensity for impulsive aggression and amygdala responses to fearful expressions in a large sample of individuals ($n = 310$) (Choe et al. 2015). However, none of these studies reported either increased responsiveness of the hypothalamus or the PAG. Although this lack likely reflects methodology, neither region is typically investigated in current fMRI work.

## Determining the Behavioral Consequences of Acute Threat System Activation: The Role of the vmPFC

The acute threat circuitry is assumed to be regulated via frontal cortical regions, particularly the vmPFC. The dominant view is that the vmPFC inhibits (''puts the brakes on'') the aggressive responses mediated by the amygdala, hypothalamus, and PAG ( Nelson and Trainor 2007; Schiller and Delgado 2010; Diekhof et al. 2011; Etkin et al. 2011). Consistent with this view, some animal studies show that lesions of the vmPFC increase aggression (Izquierdo et al. 2005), and human patients with vmPFC lesions are at increased risk for impulsive aggression (Grafman et al. 1996). In addition, there has been a report that lesions of the vmPFC show increased amygdala responses to threatening stimuli relative to comparison individuals (Motzkin et al. 2015), although other studies report that patients with vmPFC lesions show typical transient reactions to emotional stimuli (Gillihan et al. 2011). Moreover, at first pass, the data from the studies of approaching threat also support the ''brakes'' view. Increasing activity within the PAG as the threat approached was associated with decreasing activity within the vmPFC (Mobbs et al. 2007, 2009, 2010). Moreover, increasing activity within the PAG during social exchange tasks, as punishment level delivered to an unfair partner increased, was also associated with decreasing activity within the vmPFC (White et al. 2013, 2014), although not always (Strobel et al. 2011).

But other data do not support a ''brakes'' function for the vmPFC. For example, the fMRI literature indicates that the vmPFC is not involved in emotional regulation (Buhle et al. 2014). Moreover, vmPFC lesions ''protect'' the individual from the development of PTSD/depression (Koenigs and Grafman 2009). Critically, animal studies demonstrate that vmPFC lesions *suppress* amygdala activity during decision- making paradigms (Schoenbaum et al. 2006) and *decrease* fear reaction to novel threat stimuli in macaques (Izquierdo et al. 2005). Moreover, although studies with patients at increased risk for emotional lability and impulsive aggression are often assumed to demonstrate disruption in the regulatory role of the PFC, the reality is that the data are inconsistent both with respect to whether an effect is shown and, if it is shown, with respect to what region of frontal cortex is implicated (Herpertz et al. 2001; Lee et al. 2008, 2009; New et al. 2009).

Considerable work demonstrates that the vmPFC, through interactions with the amygdala/caudate, represents object or action value (Schoenbaum et al. 2011; O'Doherty et al. 2015). Therefore, rather than consider the vmPFC to be simply putting the brakes on the amygdala, it might be better to consider that it provides information on potential rewards and costs of future actions, so that optimal response choice can occur. The optimal choice might be freezing or fighting. According to this view, for example, vmPFC dysfunction reduces, not increases, amygdala responsiveness during decision making because the *integrated* functioning of these structures is allowing response choice (cf. Schoenbaum and Roesch 2005). There is an inverse relationship between PAG and vmPFC activity as a function of retaliatory punishment in the social exchange paradigms, because retaliation is associated with money lost to the participant and the vmPFC is representing this lost reward (White et al. 2013, 2014). Lesions of the vmPFC/orbital frontal cortex (OFC) increase impulsive aggression not because the aggressive response is disinhibited, but rather because the costs and benefits of engaging in impulsive aggression are not properly represented. This view places an instrumental slant on many instances of impulsive aggression; that is, although impulsive aggression may be an automatic response to an extreme threat, it may also be a selected response (as fear reactions to novel threat stimuli and responses on the TAP and PSAP are). In this regard, it is notable that the aggression shown by primates following OFC lesions correlates highly with the aggression shown *to* the primate by other primates (Bachevalier et al. 2011). In other words, the increased aggression may be just one reflection of poorer behavioral choices in the primate following the OFC lesion.

## The Role of the vmPFC in Reinforcement-Based Decision Making

Instrumental aggression is, by definition, goal-directed antisocial behavior conducted to gain a favorable outcome (e.g., another individual's money) (Berkowitz 1993). As such, instrumental aggression is mediated by the neural architecture that processes instrumental actions generally (Blair et al. 2014). An important consideration is that whether or not an instrumental action is initiated depends upon reinforcement-based decision making.

An adequate review of the extensive literature on reinforcement-based decision making is beyond the scope of the current article, particularly given its focus on impulsive aggression (see instead Schoenbaum et al. 2011; O'Doherty 2012; Rangel and Clithero 2012). Core structures involved include the amygdala, vmPFC, dorsomedial frontal cortex (dmFC), anterior insula cortex (AIC) and striatum (Schoenbaum et al. 2011; O'Doherty 2012; Rangel and Clithero 2012;). It is argued that patients with psychopathic traits are at increased risk for instrumental aggression because of a failure to process other individuals' distress (Blair 2013). The individual with psychopathic traits is more likely to choose actions that harm others (including instrumental aggression) because the action's costs (in harm to others) are represented weakly (Blair 2013). Supporting this hypothesis, amygdala responsiveness to other individuals' fear expressions is inversely associated with instrumental aggression (Lozier et al. 2014).

Behavior, however, is often classified as impulsive when it is instrumental but initiated without an adequate processing of the costs/benefits of the action (the individual ''impulsively'' grabs the small, immediate reward rather than waiting for a period of time for the much greater reward [Mischel et al. 1989] or, as a forensic example, mugs an individual despite knowledge of that person's lack of financial resources). A notable task of propensity for this form of impulsiveness is the temporal discounting (TD) task (Mitchell 1999). In this task, participants are asked to choose between an immediate reward and a delayed reward of greater value. The smaller the amount of the immediate reward that the participants will accept in preference to a larger future reward reflects their level of impulsivity (Mitchell 1999).

The appropriate representation of future reward magnitude relies on the responsiveness of the striatum (nucleus accumbens) and vmPFC (for a review, see Peters and Buchel 2011). Lesions of the vmPFC increase impulsiveness on this task (Sellitto et al. 2010) and individuals showing greater impulsivity on the task show weaker striatal responsiveness to future rewards (e.g., Ballard and Knutson

2009). Consistent with previous findings of reduced representation of reward information within striatum and vmPFC in youth with conduct disorder (CD) (Finger et al. 2008; Crowley et al. 2010; Finger et al. 2011; White et al. 2013b), youth with CD show increased impulsiveness on the TD task (White et al. 2014b).

In short, failure to adequately represent rewards will result in impulsive behavior (i.e., poorly motivated behavioral choices) including, potentially, an increased risk for ''impulsive'' aggression.

### The Role of Other Regions of the Cortex: Dorsomedial and Anterior Insula Cortices

It should be noted tha, studies have shown that frustration and social provocation evoke responses within the dmFC and AIC, as well as in the vmPFC (King-Casas et al. 2008; Rilling et al. 2008; Sanfey et al. 2008; Corradi-Dell'acqua et al. 2013; White et al. 2014a; Yu et al. 2014). It is not typically suggested that these regions are involved in the regulation of the amygdala/PAG. Instead, these regions are implicated in the representation of outcomes and response choice, particularly the avoidance of suboptimal outcomes (Alexander and Brown 2011). The suggestion is that the dmPFC responds to unexpected outcomes (cf. Alexander and Brown 2011) and the AIC/inferior frontal gyrus orchestrates potentially necessary changes in behavioral response (cf. Blair and Cipolotti 2000; Budhani et al. 2007). The functional integrity of these structures can be indexed through ''behavioral inhibition'' tasks (e.g., the Stop and Go/No-Go tasks). Impaired performance on these tasks is associated with an increased risk for impulsive aggression (Young et al. 2009).

### Conclusions

The goal of this review was to provide a brief overview of the neurobiology of impulsive aggression. In summary, the suggestion is that many cases of impulsive aggression, particularly those associated with anger, involve the recruitment of the acute threat response system (amygdala, hypothalamus, and PAG). It is suggested the impulsive aggressive response, mediated by the acute threat system, is modulated by the vmPFC. The argument is not that the vmPFC puts the ''brakes'' on the acute threat response but rather that it allows the representation of expected rewards and punishments associated with the action. This information is then utilized by other regions, perhaps particularly the dmFC in conjunction with the AIC, which will either initiate impulsive aggression or prevent it, depending upon reinforcement expectancies. The vmPFC, together with the dmFC/AIC, are involved in response choice generally. If they are compromised, behavior generally is more likely to be impulsive. There may be an increase in (impulsive) aggression as a result of this increased impulsivity.

### Clinical Significance

An understanding of the neurobiology of aggression provides an underlying framework for clinical decision making with respect to aggressive patients. This literature stresses that decisions for the patient presenting with elevated instrumental aggression should be different from those presenting with impulsive aggression. If the patient is presenting with instrumental aggression, particularly if this is accompanied by high limited prosocial emotions, current interventions are likely to be less successful. If the patient is presenting with predominantly impulsive aggression, then the current literature particularly stresses interventions that might reduce acute threat response related activity and/or improve the role of the vmPFC in modulating behavior via reward expectation representation. Moreover, the literature therefore stresses that these functional processes should be considered treatment targets. It will be important to determine whether current and future interventions influence the functioning of these mechanisms.

### Disclosures

No competing financial interests exist.

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