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Considering anger from a cognitive neuroscience perspective

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Abstract

The goal of this paper is to consider anger from a cognitive neuroscience perspective. Five main claims are made: First, reactive aggression is the ultimate behavioral expression of anger and thus we can begin to understand anger by understanding reactive aggression. Second, neural systems implicated in reactive aggression (amygdala, hypothalamus and periaqueductal gray; the basic threat system) are critically implicated in anger. Factors such as exposure to extreme threat that increase the responsiveness of these systems, should be (and are in the context of Post Traumatic Stress Disorder), associated with increased anger. Third, regions of frontal cortex implicated in regulating the basic threat system, when dysfunctional (e.g., in the context of lesions) should be associated with increased anger. Fourth, frustration occurs when an individual continues to do an action in the expectation of a reward but does not actually receive that reward, and is associated with anger. Individuals who show impairment in the ability to alter behavioral responding when actions no longer receive their expected rewards should be (and are in the context of psychopathy) associated with increased anger. Fifth, someone not doing what another person wants them to do (particularly if this thwarts the person's goal) is frustrating and consequently anger inducing. The response to such a frustrating social event relies on the neural architecture implicated in changing behavioral responses in non-social frustrating situations.

Introduction

Anger is often considered to be a response to a perceived threat to oneself or to another. It is also a response to frustration; frustration has long been recognized as a trigger for anger and eventual aggression [1].

The goal of this paper is to provide a view of anger that is consistent with contemporary cognitive neuroscience. However, it is not possible to provide a full account of anger since, as an experienced emotion, it would be necessary to have an account of conscious experience, something that is a long way from being achieved. Because of this, an alternative approach will be adopted in this paper. An important correlate of anger, reactive aggression, will be analyzed as a way of considering anger.

Reactive aggression and the basics of anger

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. The aggression is often accompanied by anger and can be considered "hot". It is initiated without regard for any potential goal.

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Reactive aggression appears to be exhibited by all mammalian species [2, 3]. It is part of the mammalian gradated response to threat. Low levels of danger from distant threats induce freezing. Higher levels of danger from closer threats induce attempts to escape the immediate environment. Higher levels of danger still, when the threat is very close and escape is impossible, initiate reactive aggression [2].

Animal work indicates that this progressive response to threat is mediated by a basic threat system 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; [3, 4]. This system is organized in a hierarchical manner such that aggression evoked by stimulation of the amygdala is dependent on the functional integrity of the medial hypothalamus and the periaqueductal gray but aggression evoked by stimulation of the periaqueductal gray is not dependent on the functional integrity of the amygdala [3, 4]. This neural system, amygdala-hypothalamus-periaqueductal gray is thought to mediate reactive aggression in humans also [3–5]. Certainly, imminent as opposed to distal threat is associated with significantly greater periaqueductal gray activity [6]. This paper will consider whether this neural circuitry might be considered the basis of anger.

The neural systems involved in mediating the basic response to threat, amygdala-hypothalamus-periaqueductal gray, are regulated by several regions of frontal cortex; orbital, medial and ventrolateral frontal cortex [5]. Indeed, a gradated response within medial frontal cortex occurs, increasing proportionally with the individual's retaliative reactive aggression [7].

Following the argument above, whether these regulatory systems may also be involved in mediating human anger will be considered. There certainly already is evidence implicating some of them in the anger response following human imaging work [see below; 8, 9].

In this paper, a cognitive neuroscience of anger will be developed from three main premises:

1. If anger is a response to perceived threat is increased threat, acutely and chronically, associated with increased anger? If it is, what are the neural consequences of acute and/or chronic threat?
2. There are frontal systems that are important for the regulation of the basic response to threat; i.e., orbital, medial and ventrolateral frontal cortex [5]. Behavioral expressions of anger can be accompanied by a sense of loss of control. Do dysfunctions within those neural systems important for regulating the basic threat response increase the risk for expressed anger?
3. Frustration occurs when an individual continues to do an action in the expectation of a reward but does not actually receive that reward. The individual may expect the reward because he/she does not know that the reinforcement contingencies have changed; the action can no longer elicit reward. Does it therefore follow that the more able that the individual is to change their behavior in response to this contingency change, the less frustrated they should feel and the less anger they should experience. One way to index the ability to change behaviors following contingency change is through reversal learning paradigms. Is impaired response reversal associated with increased anger?

It is to be hoped that by working through these premises, it will be possible to develop the beginning of a cognitive neuroscience of anger. One way to do this is through work with patient populations; both neurological and psychiatric. There are a variety of neurological and psychiatric conditions that are at increased risk for anger, rage and reactive aggression. These include posttraumatic stress disorder [10], borderline personality disorder [11],

psychopathy [12], and "acquired sociopathy" following damage to orbital frontal cortex [13, 14]. This approach will be adopted below.

Threat and anger—Is anger a response to perceived threat? Certainly, reactive aggression is a consequence of perceived threat; when a threat is very close and escape is impossible, reactive aggression will be displayed [2]. It appears that the same can be said about anger. Individuals placed within threatening environments exhibit higher levels of anger and irritability [15]. As mentioned above, the amygdala-hypothalamus-periqueductal gray is thought to mediate the basic response to threat [3, 4]. If this circuit is implicated in anger, we should see perturbations in these systems following exposure to threat that might be causally related to anger.

One way of addressing the neural consequences of acute and/ or chronic threat is to consider the neural systems implicated in the psychiatric disorder associated with the response to experienced threat; post traumatic stress disorder (PTSD). Considerable data from work with patients with post traumatic stress disorder indicates that this disorder is associated with elevated amygdala responsiveness [16, 17] though, it should be noted that there has been, as yet, little investigation into whether the hypothalamus and periaqueductal gray are also hyper-responsive in patients with PTSD. There are data indicating an increased risk for reactive aggression in patients with post traumatic stress disorder [10]. Moreover, anger and rage are prevalent emotions in individuals experiencing post traumatic stress disorder [18, 19], so prevalent that they are considered part of the clinical description of the disorder. In short, in line with the position developed above, perceived threat alters the responsiveness of the basic threat circuitry (amygdala-hypothalamus-periaqueductal gray) and this alteration is associated with an increased risk for anger.

There is a second disorder consistently associated with increased amygdala responsiveness, though this does not appear to be due to prior threat exposure. Thus, data suggests that patients with borderline personality disorder show elevated amygdala responses to threat related cues [20, 21]. Interestingly, patients with borderline personality disorder are also at considerably elevated risk for anger and reactive aggression [22].

Moreover, there are data from work with healthy populations that also support this suggestion. Thus, a predisposition to anger has been positively associated with an increased amygdala response to masked fearful expressions [23] and even the presentation of the word "no" [24]. Moreover, an increased predisposition to anger has also been positively associated with increased amygdala volume [25].[i]

Emotional regulation and anger—Several regions of frontal cortex are important for the regulation of emotion, including the regulation of the basic response to threat. These include orbital, medial and ventrolateral frontal cortex [5, 27, 28]. Early accounts of the regulation of emotion assumed a single inhibitory system [27]. However, it now appears plausible that there are multiple systems that contribute to the emotional responsiveness of the basic threat system. For example:

There are regions of frontal cortex that appear to project excitatory connections to, potentially inhibitory interneurons within the amygdala, leading to a reduction in amygdala

[i]It is worth briefly considering the relationship between threat, anger and fear. Threats lead to fear as well as anger. Indeed, the basic threat circuitry outlined above (amygdala-hypothalamus-PAG) is involved in fear as well as anger. The avoidance behavior associated with fear relates to a lesser activation of this circuitry than that resulting in the reactive aggression associated with anger. It has been argued elsewhere that threat based reactive aggression is significantly less common in individuals with psychopathy than in healthy individuals, due to their amygdala dysfunction, but that frustration based reactive aggression is significantly more common due to difficulties with reinforcement learning [26].

activity [29]. It is possible that such connections are recruited during emotional suppression paradigms where there appears to be direct frontal suppression of the amygdala [30, 31].

Considerable data using reappraisal paradigms attest to a role for attentional manipulation of emotional stimuli such that the emotional responses to these stimuli can be suppressed [28]. If the individual attends to non-emotional features of a stimulus, the representation of these non-emotional features, following models of attention as representational competition [32], will interfere with the representation of the emotional features of the stimulus and thus reduce consequent emotional responding to these features [33, 34]. This form of attentional emotional suppression also occurs when attention to task relevant features of a stimulus interferes with the representation of the emotional features of the environment [31, 35].

It is notable that frontal regions implicated in the regulation of emotion, orbital, medial and ventrolateral frontal cortex, have also been implicated in the anger response. Thus, anger induction studies have found this emotion associated with increased activity in these regions [8, 9]. Indeed, it is possible that the expression of anger occurs when these regulatory regions have been overwhelmed due to the salience of the anger cue (or the fact that their operation was compromised in the individual). As such, the sense of a loss of control sometimes associated with the anger experience may reflect awareness within the individual of the reduced operational efficiency of these systems.

If these regions of frontal cortex are important for the regulation of emotion, including the regulation of the basic response to threat, it can be expected that dysfunction within these regions should be associated with increased anger. This is what is seen. Patients with acquired lesions to ventromedial and ventrolateral frontal cortex may present with “acquired sociopathy” [13, 14]. Such patients present clinically with impaired emotional regulation though this has not been formally tested. They also present with considerable difficulties in the regulation of anger, rage and reactive aggression [13, 14, 36].

Frustration and anger

An interesting disorder to consider with respect to frustration based anger and reactive aggression is psychopathy. The risk factors for increased anger/ reactive aggression considered above relate to emotional hyper-responsiveness; increased basic threat responsiveness or under-regulation of this basic threat responsiveness. However, while individuals with psychopathy show increased risk for reactive aggression [12, 37], they do not show increased responsiveness of the basic threat circuitry. Thus, considerable neuropsychological work has shown that individuals with psychopathy show significant impairment on tasks which rely on the functional integrity of the amygdala; e.g., aversive conditioning, passive avoidance learning, augmentation of the startle reflex by threatening visual primes and fearful face recognition [for reviews of this literature, see 38, 39]. Moreover, a variety of neuroimaging studies with both adults and children with psychopathic tendencies have shown reduced amygdala responses to threat stimuli [40–42]. In short, it is unlikely that increased risk for reactive aggression in psychopathy relates to increased responsiveness of the basic threat circuitry since core components of this circuitry appear to be *under* rather than *over* responsive [see 26].

The suggestion is that, since responsiveness to threat based stimuli is reduced in individuals with psychopathy, the increased risk for reactive aggression seen in psychopathy reflects an increased risk for frustration rather than threat based reactive aggression. However, it should be noted that while it is clear that there is an increased risk for reactive aggression in psychopathy [12, 37], no empirical studies have yet attempted to disentangle whether this reactive aggression is threat or frustration based.

Frustration occurs when an individual continues to do an action in the expectation of a reward but does not actually receive that reward [1]. The individual may expect the reward because he/she does not know that the reinforcement contingencies have changed; the action no longer engenders reward. FMRI studies investigating the response to frustration have all adopted this form of task structure whereby the participant does not receive the expected reward [43–45]. These studies have reported that frustrating events, the absence of expected reward, are associated with reductions in activity within striatum [44] and that this is particularly marked in substance abusing populations [45]. This would be expected from the prediction error literature [see below: 46, 47]. These data might suggest therefore that impairments in the ability to detect changes in reinforcement contingencies might be associated with increased anger.

Two tasks which index an individual's ability to alter their responding following a contingency change are behavioral extinction [48] and reversal learning [49]. In behavioral extinction paradigms, the individual learns to make a response to a stimulus in order to gain a reward but then this behavior is no longer rewarded. In reversal learning paradigms, the individual initially learns to make a response to gain a reward. After a number of trials, the reinforcement contingency changes such that the previously correct response no longer results in reward, and a new response must be learned to achieve the reward. Individuals with psychopathy are impaired in both behavioral extinction [50] and response reversal [51, 52].

Regions that have been implicated in response reversal in both animal and human studies include orbital/ ventromedial (Brodmann's Area 10 and 11), inferior (BA 47 and 45 – typically extending into anterior insula) and dorsolateral frontal cortex, dorsal anterior cingulate cortex (BA 32) and striatum [53–55]. Thus, work with monkeys has shown that lesions that include orbitofrontal cortex lead to impaired behavioral extinction [56] and reversal learning [53]. Similar work with humans has also observed that lesions of orbital/ ventromedial frontal cortex lead to impairment in behavioral extinction [57] and reversal learning [58].

Studies have indicated a role for ventromedial frontal cortex (including, in some studies, more superior regions of BA 10) in encoding the value of Pavlovian conditioned stimuli [59, 60]. Similar regions of ventromedial frontal cortex have shown activation to reinforcement outcome information in stimulus-reinforcement based decision making tasks [61–64] or in tasks where the outcome information is explicitly supplied to the participant [65, 66]. In addition, and presumably related, to the role of medial orbitofrontal cortex in the representation of reinforcement information, it is also sensitive to prediction errors; i.e., situations where an anticipated reward does not occur [67, 68]. Thus, during reversal learning, ventromedial frontal cortex shows a significant *reduction* in activity during reversal errors (trials when a previously rewarded response is now punished) [54]. It is argued that this signaling in ventromedial prefrontal cortex may be needed for the detection of contingency change and thus the initiation of reversal learning [54].

The functions of dorsomedial, lateral and inferior frontal cortex in the context of reversal learning appear to relate to orchestrating the change in behavioural response following a change in reinforcement contingency [54]. Dorsomedial frontal cortex has been implicated in monitoring response conflict [69] and error detection [the discrepancy between actual and intended events] [70]. Dorsomedial together with lateral frontal cortices are implicated in top down attentional control [71]. Inferior frontal cortex has been implicated in altering motor responses [54]. Indeed, impairments in action selection are seen after lesions of the inferior frontal cortex [72, 73].

In short, problems with reversal learning and thus an increased risk for frustration and reactive aggression/ anger might result from either difficulties in either the role of ventromedial frontal cortex in detecting the contingency change or in the role of dorsomedial/ lateral/ inferior frontal cortex in orchestrating the immediate change in behavioural response. In the case of psychopathy, the problem appears to lie in the role of ventromedial prefrontal cortex dysfunction in psychopathy [39]. This is thought to lead to the apparent "impulsivity" in individuals with psychopathic traits; these individuals are less able to use appropriate reinforcement expectancies to guide their behavior and thus appear more impulsive. Indeed, a series of studies have revealed deficient signaling of reinforcement information within ventromedial frontal cortex in individuals with psychopathic traits [40, 74–76] Moreover, direct data from children with psychopathic tendencies performing a reversal learning paradigm has been obtained [75]. In this study, the youth with psychopathic tendencies failed to show the reduction in ventromedial frontal cortex activity following the change in reinforcement contingency signaled by a punished reversal error. In short, the suggestion is that individuals with psychopathic tendencies show higher levels of reactive aggression because they are more frequently frustrated than comparison individuals. They are more frequently frustrated than comparison individuals because their ability to represent reinforcement information (and learn from changes in reinforcement contingency) is impaired and thus they are less likely to make decisions that will successfully achieve their goals.

Interestingly, there has been some work suggesting that individuals who are particularly prone to frustration/ anger show increased responses following the omission of reward within dorsolemedial, lateral and inferior frontal cortices [43]; in other words, within those regions important for orchestrating immediate changes in behavioral response. This might suggest that activity within these regions relates to experienced anger (see also below).

Anger in the social context

One typical stimulus for the expression of anger is the sight of another individual engaging in a behavior that the observer wishes that this individual would not commit [77]. Indeed, it has been shown that individuals punish those who do not cooperate and that this punishment appears to relate to the anger than you feel towards them [78, see also 79]. On this basis, there have been claims that it is the threat of other's anger/ punishment that enforces social norm compliance generally [80]. However, it is important to note here that there are different types of norms. At the very least, care-based (involving harm to others; e.g., hitting another), conventional (involving social disorder; e.g., talking in class), disgust based (often relating to proscribed sexual activities) and fairness based norms (involving resource allocation/ cooperation decisions) can be distinguished [39, 81]. The role of dissociable emotional learning systems for the development of these different forms of norms has been described elsewhere [39]. However, with respect to this paper, it is important to note that the display of anger appears less relevant to care-based norm development/ enforcement. Care based transgressions initiate empathy induction and references to the victim in care-givers rather than anger (anger is typically shown to individuals committing conventional transgressions); [82]. Moreover, punishment decisions with respect to transgressors of care based norms relate to activity within the amygdala, ventromedial prefrontal and posterior cingulate cortices [83], regions implicated in processing care based norms [39] but not regions involved in punishment decisions with respect to cooperation norm violations [84, 85].

In short, displays of anger appear far more important for the development/ maintenance of conventional and fairness/ cooperation norms than care-based norms. But what is the relationship of anger with respect to norm violations to the discussion of the neural systems implicated in anger above? According to one recent model, the recalibration theory of anger,

> "anger is produced by a neurocognitive program engineered by natural selection to use bargaining tactics to resolve conflicts of interest in favor of the angry individual. The program is designed to orchestrate two interpersonal negotiating tactics (conditionally inflicting costs or conditionally withholding benefits) to incentivize the target of the anger to place greater weight on the welfare of the angry individual. Individuals with enhanced abilities to inflict costs (e.g., stronger individuals) or to confer benefits (e.g., attractive individuals) have a better bargaining position in conflicts" and thus will be "more prone to anger, prevail more in conflicts of interest, and consider themselves entitled to better treatment" [p. 15073; 86].

Such an account might suggest that this naturally selected neurocognitive program might organize some of the neuro-cognitive circuitry described above (the basic threat system for example). But need the existence of such a program be postulated?

As noted above, frustration, and consequently anger, occurs when an individual engages in a behavior in the expectation of a reward but does not actually receive that reward. Expectations of reward can occur on the basis of the individual's own motor action or another individual's behavior. In other words, asking another individual to do something on the assumption that they will do it and then them not doing it, is frustrating and anger inducing. Why should stronger (males in particular) and more attractive (females in particular) individuals be more prone to anger [cf. 86]? While this might relate to the activity of a dedicated neurocognitive program involved in interpersonal conflict resolution, it appears perhaps more plausible that it relates to the expectations of such (high status) individuals. As the data demonstrate [86], such individuals have greater expectations that others will do as they are requested. Consequently, if these expectations are violated, they will experience greater frustration and a higher propensity for anger.

This is worth considering with respect to conventional transgressions (e.g., talking in class). As noted above, conventional transgressions are significantly more likely to induce anger in care-givers than care based transgressions [82]. Conventional rules are proscriptions of authority/ high status figures as to how subordinate/ low status individuals should behave (children should not talk in class and personal assistants should not put their feet up on the CEOs desk during a meeting); [39]. They are rules describing the expectations of authority/ high status figures regarding the behavior of subordinates/ low status individuals. The thwarting of these expectations should lead to frustration and anger.

But what about fairness/cooperation norms and, critically, the neural systems that organize this anger response to fairness/cooperation norm violations. While fairness/cooperation norms frequently involve scenarios where the individuals involved are of comparable status, data indicates that in cooperative scenarios participants expect resources to be distributed equally [78]. As noted above, failure to distribute resources equally leads to anger and, if possible, retributive punishment by those unfairly treated [78]. At the neural level, the individual shows activation within anterior insula and dorsomedial and lateral frontal cortices [87, 88]. Notably all three of these regions show clear engagement in reversal learning and behavioral extinction paradigms [54, 89]; see above. Indeed, the propensity to show activity within these regions to frustrating circumstances may relate to the propensity for experienced frustration/ anger [43].

In short, the regions that organize the anger response to fairness/cooperation norm violations are those that organize the motor change following non social frustrating events. As such, rather than assume the existence of a dedicated program for social conflict resolution, one might consider that anger to the frustrating behavior of another recruits the same neural systems as anger to frustrating events more generally.

Conclusions: The cognitive neuroscience of anger—There are five basic suggestions made in this paper: First, reactive aggression is the ultimate behavioral expression of anger and, as such, it is possible to learn about the cognitive neuroscience of anger by understanding the cognitive neuroscience of reactive aggression.

Second, the systems seen in other mammalian species to mediate reactive aggression (amygdala, hypothalamus and periaqueductal gray; the basic threat system) are critically implicated in reactive aggression in humans also. As such, they are also critically implicated in anger. Factors that increase the responsiveness of these systems, such as exposure to prior trauma, should be, and are (cf. post traumatic stress disorder), associated with elevated incidences of anger and reactive aggression.

Third, regions of frontal cortex have been implicated in the regulation of the activity of the basic threat system. As such, if they become dysfunctional, there is likely to be increased anger and reactive aggression. This is seen in neurological patients following lesions of orbital frontal cortex.

Fourth, frustration has long been recognized as a trigger for anger. It occurs when an individual continues to do an action in the expectation of a reward but does not actually receive that reward. The ability to alter behavioral responding when actions no longer receive their expected rewards can be indexed through behavioral extinction or reversal learning paradigms. Individuals with psychopathy show profound impairment on such tasks and it has been argued here that this dysfunction relates to their increased risk for frustration based reactive aggression.

Fifth, frustration can occur not only when an action turns out unexpectedly and a reward/goal is not achieved but also when another person's behavior is unexpected and a reward/goal, dependent on that person's action, is not achieved. The response to frustrating social events appears to rely on the neural architecture implicated in orchestrating a change in response in non-social frustrating situations.

It is hoped that these suggestions begin the foundation for a cognitive neuroscience of anger. It is a particularly important emotional response to understand given that inappropriate levels of its expression are associated with so many psychiatric conditions.

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