Deconstructing Anger in the Human Brain

Gadi Gilam and Talma Hendler

Abstract Anger may be caused by a wide variety of triggers, and though it has negative consequences on health and well-being, it is also crucial in motivating to take action and approach rather than avoid a confrontation. While anger is considered a survival response inherent in all living creatures, humans are endowed with the mental flexibility that enables them to control and regulate their anger, and adapt it to socially accepted norms. Indeed, a profound interpersonal nature is apparent in most events which evoke anger among humans. Since anger consists of physiological, cognitive, subjective, and behavioral components, it is a contextualized multidimensional construct that poses theoretical and operational difficulties in defining it as a single psychobiological phenomenon. Although most neuroimaging studies have neglected the multidimensionality of anger and thus resulted in brain activations dispersed across the entire brain, there seems to be several reoccurring neural circuits subserving the subjective experience of human anger. Nevertheless, to capture the large variety in the forms and fashions in which anger is experienced, expressed, and regulated, and thus to better portray the related underlying neural substrates, neurobehavioral investigations of human anger should aim to further embed realistic social interactions within their anger induction paradigms.

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Contents

1 Introduction

> *Anybody can become angry, that is easy; but to be angry with the right person, and to the right degree, and at the right time, for the right purpose, and in the right way, that is not within everybody's power and is not easy.*
>
> Aristotle

As exemplified in the Iliad, Homer's war epic depicting Achilles's wrath in relation to the events of the Greek-Trojan war, anger is at the core of what it means to be human. Indeed, people report experiencing anger on a daily basis and consider it as one of the most prototypical exemplars of an emotion (Fehr and Baldwin 1996; Scherer and Tannenbaum 1986). Yet, defining anger as a single psychobiological phenomenon has posed considerable theoretical and experimental difficulties. In this chapter, we provide a psychological account of what anger is and review how the subjective experience of anger in healthy humans has been investigated thus far using neuroimaging techniques. We conclude by suggesting the scaffolding for the reconstruction of an "angry brain" which may take into consideration the multi-dimensionality of the anger construct.

2 What Is Anger?

There is much controversy on the theoretical conceptualization of anger, as on defining emotion in general, and while a survey of the emotion literature breaches the scope of this chapter, two renowned theoretical considerations of anger are

briefly noted. According to Berkowitz's Cognitive-Neoassociationistic theory (Berkowitz 1990), a primitive form of anger is automatically triggered upon a provocation through an associative network of components including feelings, thoughts, memories, and most emphasized, physiological, and expressive motor reactions. Only with the temporal yet rapid unfolding of the emotional instance, the affected person makes appraisals, interpretations, and causal attributions which enable to construct complex high-order thoughts and feelings related to the actual emotion of anger. Embedded within these later stages is the ability to control and regulate anger and reactions to it. According to Averill's Social-Constructionist theory (Averill 1983), anger is regarded as a social syndrome which cannot be deconstructed into subclasses of physiological, cognitive, or any other element. Averill stresses that social rules govern the organization of the various elements of anger, which is considered in itself as a complete response of the person, and because of the great variety in these various elements, influenced by personal and situational circumstances, it is impossible to define a typical angry experience. Anger can thus be understood only within its specific contextual framework.

Though a clear cognitive–physiological versus social perspectives distinct Berkowitz's and Averill's theories, both agree that there is an intensity element to anger occurrence, from annoyance and irritation to anger and rage. More importantly, Averill and Berkowitz agree (c.f. Berkowitz and Harmon-Jones 2004) in referring to anger as an *emotional syndrome* because of its multidimensional complexity and that a temporal unfolding of the emotion is apparent in its construction. They also both point to the regulatory processes that may intervene along this temporal dynamic. Although theoretical disagreement on the nature and definition of anger remains, the complex and dynamic conceptualization of anger is agreed upon and supported by empirical findings.

2.1 Causes of Anger

Antecedents and instigators of anger may be sorted into three primary categories which support both Berkowitz and Averill's theoretical frameworks. Various exemplars of these categories reappear in anger-inducing paradigms used in the laboratory. These categories are as follows: (1) real or imagined threat such as physical or psychological pain, but also more trivial environmental aversive conditions such as aversive temperature and even polluted air (c.f. Berkowitz and Harmon-Jones 2004), (2) frustration due to goal obstruction (e.g., Carver 2004; Szasz et al. 2011), and (3) perceived personal offense due to unfair treatment, violation of social norms, insults, rejections, criticism, and the likes (e.g., Denson et al. 2009; Memedovic et al. 2010; Porath and Erez 2007; Srivastava et al. 2009).

The first category relating to threat reflects the most basic form of anger, regarded as the instinctive survival response which triggers the fight feature of the fight or flight reaction (Anderson and Bushman 2002; Siever 2008). Reactive aggression triggered by a threat is perhaps the most typical behavioral expression of

anger, and thus, anger has been traditionally viewed as interchangeable with aggression. Anger may indeed be pivotal in the generation and propagation of violent acts against the self and others. Nevertheless, aggressive acts may be perpetrated without any trace of anger, and at the same time, anger is an emotional construct in its own right, not necessarily a harbinger of aggression. In contrast, a profound interpersonal foundation is apparent in the third category. In accordance, the expressions of anger have evolved from their primitive forms and adapted to socially accepted norms (Averill 1983; Baumeister et al. 1990; Fehr and Baldwin 1996). For example, people would probably not shout in the middle of a restaurant at a rude waiter, but rather restrain themselves and choose more accepted forms of rebuttal, such as minimizing the tip. This suggests that in order to realistically capture the multifaceted concept of anger, experimental designs should incorporate an interpersonal social interaction and try to dissociate between the experience and the expression of anger.

2.2 Anger Experience

During the actual experience of anger, a person is commonly described as having a cluster of physiological, cognitive, and behavioral attributes which are directly related to the temporal dynamics of anger. Physiologically, an angry experience is characterized by an increase in respiration, blood pressure, heart rate, skin and body temperature, and skin conductance (Stemmler 2010) indicating the involvement of both sympathetic and parasympathetic systems of the autonomic nervous system. Other bodily changes include specific facial features and a general muscular tightness (Berkowitz and Harmon-Jones 2004; Scherer and Tannenbaum 1986). Anger is thus generally considered as a very arousing emotional condition.

A negative cognitive appraisal of circumstances characterizes anger. Obsessive and loopy thinking, planning of revenge and retaliation, and judgmental and derogative labeling are just some forms of angry cognitions (Fehr and Baldwin 1996). Such intrusive negative provocation-focused thought patterns during anger are termed together as *rumination* (Rusting and Nolen-Hoeksema 1998) during which people masticate the causes and consequences of the angry event. Rumination also tends to further intensify and prolong the angry experience.

Behaviorally, an angry person is in a general nervous attitude with a proneness to some form of physical or verbal aggression (Deffenbacher et al. 1996). Arguments with yelling and screaming are also very common during anger episodes. However, other expressions may be less confrontational such as using conflict resolution, withdrawing from the situation, or implementing relaxation techniques. Studies have generally found a myriad of behavioral expressions of anger which support Averill's (1983) assertion that "given an adequate provocation, nearly any response, and even no response, can count as a manifestation of anger" (there, p. 1147).

While physiological responses to anger are generally quite short and last up to several minutes, the subjective experience of day-to-day anger typically lasts for about half an hour, during which rumination is common, though duration is correlated with intensity (Potegal 2010). The temporal dynamics of anger experience are also characterized by an escalating property, in which annoyances and irritations accumulate over time, and behavioral responses that begin with mild requests may reach strong angry outbursts (Baumeister et al. 1990). Similar to the folktale of "the straw that broke the camel's back," there seems to be a nonlinear effect in the trajectory of anger in which at the extreme end, a sense of loss of control and irrationality captures the essence of a person's experience, and it is more difficult to be soothed or distracted. While anger rises quickly and declines slowly, it may be terminated by natural decay, quenching, or catharsis, all of which may be considered as forms of anger regulation.

2.3 Anger Regulation

The involvement of processes that control and regulate the experience and expression of anger emerges as a crucial element embedded within this socio-emotional phenomenon. Similar to Aristotle's citation above, Gross (1998) generally defined *emotion regulation* as "the processes by which individuals influence which emotions they have, when they have them, and how they experience and express these emotions" (there, p. 275). Theoretical accounts differ in their view regarding the relation between emotion generation and regulation, as some claim that regulation is an inherent part of the generation process while others separate these two processes, but it is generally accepted that they are both critical in the construction of the emotional episode as it unfolds over time (Gross and Barrett 2011), and this is apparent in our description of anger thus far. Emotion regulation processes or strategies may be automatic or controlled, implicit, or explicit and may modulate the emotion at any stage during the evolvement of its experience and expression. There are many different strategies to regulate emotions, yet *cognitive reappraisal*, in which one changes or reinterprets how she thinks about an emotional situation, has been studied the most.

Examples of laboratory experimentation on anger down-regulation suggest that when facing or recalling an anger provocation, using cognitive reappraisal rather than suppression or rumination (Memedovic et al. 2010; Ray et al. 2008; Szasz et al. 2011) has led to a decrease in reported anger experience and reduced maladaptive cardiovascular response. Other accounts have shown a large variety in actions one may take to cope with anger (Deffenbacher et al. 1996). For example, some actions may be conciliatory in their nature, such as reciprocal communication and talking it over, while other actions may try to create distance and avoidance from the angering stimuli, such as detachment and time-outs; still another set of actions may focus on the physiological aspect, such as relaxation or drug

and alcohol consumption. It is also clear that some of these actions are more adaptive and healthy than others.

2.4 *Consequences of Anger*

Anger may have detrimental effects on our lives. It is related to poor quality of life, with people high in trait anger—that is the tendency and frequency of experiencing anger on a daily basis—having impaired psychological and social well-being (Phillips et al. 2006). Anger is implicated in negative health outcomes, most notably in cardiovascular disease (Williams 2010). For example, unrestrained expression or chronic suppression of anger affects essential hypertension and coronary heart disease. Anger irregularity is involved in many psychopathologies, such as psychotic, affective, and personality disorders (Novaco 2010). Even in anxiety disorders such as *Post-Traumatic Stress Disorder* (PTSD), related primarily to abnormal fear, there is a well-documented anger dysregulation which hampers functionality. Anger may also have debilitating effects on cognitive processes, such as in task performance and creativity (Porath and Erez 2007) and judgment and decision making (Lerner and Tiedens 2006).

Surprisingly, although experiencing anger and being the target of another's anger are primarily negative, some episodes of anger are positively evaluated (Averill 1983; Baumeister et al. 1990). Indeed, anger is adaptive and functional and has several positive aspects. It is critical for communicating an offensive event and thus has a role in maintaining status quo. Anger is also an important motivator for taking action and approaching rather than withdrawing away from a possible or actual confrontation (Berkowitz and Harmon-Jones 2004). This may be instrumental in achieving a wide variety of goals. For example, anger has a pivotal role in negotiations, and under certain conditions, expressing anger may lead to beneficial resolutions (Van Dijk et al. 2008). Moreover, anger together with disgust underlies *moral outrage*, the emotional reaction to a perceived moral transgression inflicted by others upon others (Salerno and Peter-Hagene 2013).

3 The "Angry Brain"

Disentangling the causes, consequences, experience, and expression of anger portrays a contextualized multidimensional construct consisting of physiological, cognitive, subjective, and behavioral components. Given the heterogeneous depiction of anger, research on the neural substrates of anger should try to appreciate not only whether and to what extent anger occurs, but even more so what are the forms and fashions in which anger is induced, experienced, expressed, and regulated. For obvious reasons, animal research has been preoccupied with

aggression as a behavior rather than the subjective experience of anger. Cannon and Bard's (Bard 1928) classical studies on decorticated cats showed that the hypothalamus is essential for expressing "sham rage" (i.e., aggressive behavior without anger). Seventy-years later, Panksepp (1998), based mostly on studies in rodents, suggested a primitive neural basis for anger shared by all vertebras which in addition to the hypothalamus included the amygdala and periaqueductal gray (PAG). These brain regions seem to be involved in the rapid identification and response to threat in the environment, and thus assumed to have an essential role in the generation of anger and propagation of aggression, which accompany the fight reaction of the fight or flight response. Introduction of noninvasive brain mapping methodologies such as Positron Emission Tomography (PET) and functional Magnetic Resonance Imaging (fMRI) advanced studies to search for the "angry brain" in humans.

3.1 Angry Faces Studies

Neuroimaging studies on the neural substrates of human anger can be generally divided into three types as far as how anger was evoked. The first set of studies used images depicting angry faces. The most robust finding of early studies was that unlike rodent studies, the amygdala did not seem to have a specific involvement in the neural processing of angry faces (e.g., Blair et al. 1999). Recent meta-analyses on hundreds of neuroimaging studies on emotional faces confirm the strong specificity of the amygdala in processing fearful faces, though also associated with both sad and happy faces (Costafreda et al. 2008; Fusar-Poli et al. 2009). On the other hand, angry faces were associated with neural response in regions comprising the middle frontal gyrus (MFG), anterior cingulate cortex (ACC), inferior frontal gyrus (IFG), parahippocampal gyrus (PHG), claustrum, insula, middle temporal gyrus, fusiform gyrus (FFG), and occipital gyrus. It was suggested that while visual regions such as the FFG might be generally relevant for perceptual processing of facial stimuli, paralimbic and insular regions might be involved in processes associated with the generation of anger (though perhaps more relevant in this case is the generation of a general state of arousal), whereas more frontal regions might be involved in processes associated with the conscious experience of the emotion. Nevertheless, these regions were not uniquely associated with angry faces, but seemed to be differentially involved in processing other emotions expressed in human faces. Notwithstanding, more recent studies that were not included in these meta-analyses have shown the involvement of amygdala activation in processing angry faces, especially when considering idiosyncratic personality differences. For example, it was shown that increased amygdala activity (Beaver et al. 2008) and reduced functional connectivity between amygdala and ventromedial prefrontal cortex (vmPFC) (Passamonti et al. 2008) in response to angry faces were correlated with individual differences in behavioral approach, an orientation associated with anger and aggression as mentioned above. Although the use of faces enables highly

standardized stimuli across and within subjects, such static stimuli clearly do not capture the complex nature of anger experience, rather enable to investigate the neural mechanisms mediating the perception and recognition of anger in human faces.

3.2 *Self-Generated Anger Studies*

The second set of studies used self-generation of anger by recollecting and imagining personal autobiographic memories or scripted scenarios of angry experiences. PET studies on autobiographical memories of anger (e.g., Damasio et al. 2000; Kimbrell et al. 1999) identified regions in the PFC, especially in the ventral-orbital regions, as well as ACC, temporal poles, regions of the medial temporal lobe (MTL), thalamus and hypothalamus, insula as well as regions in the brainstem and cerebellum. The involvement of the temporal poles in deducing the content of another person's mental state (i.e., mentalizing; Denny et al. 2012) might reflect the engagement in a social interaction during the recollected angry memories. However, the temporal poles as well as the MTL are involved in retrieving declarative memories (Squire et al. 2004) which seems essential in the current paradigm. A recent fMRI study focused on anger regulation via reappraisal and rumination of the autobiographic angry memory (Fabiansson et al. 2012) found activations in orbito-frontal cortex (OFC), IFG, amygdala, thalamus, insula, putamen/caudate shared by regulation strategies. In addition, while reappraisal was more successful in diminishing the subjective experience of anger, there was a specific positive functional coupling between IFG and both amygdala and thalamus during rumination which might portray the failure of such anger-focused thought pattern in attenuating the emotional experience.

While such recollection paradigms enable a more personalized reverberations of anger, these recollections are not entirely standardized across subjects. For example, in one study (Kimbrell et al. 1999), some events involved property loss, others involved being wrongly blamed, and still others generally involved verbal arguments. Such recollections might also be prone to confounds of memory biases and limited introspective insight. A PET study using scripted and more controlled scenarios to elicit the imagined anger experience showed that an unrestrained scenario in which one acts aggressively to express anger was associated with decreased activity in vmPFC and increase in ACC compared to a neural scenario (Pietrini 2000). A more recent fMRI study on social emotions broadly defined similarly found that compared to neutral events, scripted events of social rejection and criticism, which were associated with reports of anger, sadness, and shame, engaged increased activity in vmPFC as well as thalamus, amygdala, precuneus, and posterior cingulate cortex (PCC; Frewen et al. 2011). And yet, these are internally generated paradigms of anger induction and thus still lack the fundamental bluntness of actually being provoked.

3.3 Anger Induction Studies

The third and final set of studies tried to induce anger directly. In the first such study (Denson et al. 2009), participants were requested to solve difficult anagrams and say out loud through a microphone the correct answer or say "no answer" if they did not know the answer. Anger was induced by the experimenter who interrupted participants two times requesting them to speak louder and on a third time stated in a rude and condescending tone of voice "Look, this is the third time I have had to say this! Can't you follow instructions?" The analysis was based on contrasting a baseline period before and after the provocation, during which there was increased activity in the medial and lateral PFC (mPFC and lPFC, respectively), insula, thalamus, hippocampus, ACC, and PCC, of which the dorsal ACC (dACC) positively correlated with self-reported anger and trait aggression and the insula, hippocampus, rostral ACC, and PCC positively correlated with self-reported angry rumination. A very similar pattern of activation was apparent during a condition of angry rumination, during which activity in the mPFC also positively correlated with self-reported angry rumination. A subsequent study asked participants to control their anger in view of such insults and found an increase in self-reported anger compared to baseline, but a smaller effect size compared to the previous study (Denson et al. 2013). A similar pattern of brain activity emerged including the dACC, dorsal mPFC and lPFC (dmPFC and dlPFC, respectively), insula, thalamus, amygdala, and brainstem. Dorsal regions of the PFC and the insula positively correlated with self-reported anger control and negatively correlated with self-reported anger. The brain pattern of anger control was also characterized by a functional coupling between the amygdala and regions of the PFC including dlPFC, dACC, and OFC which may reflect the efforts of PFC regions to exert control over the angering provocation. While these provocation-based anger studies incorporate an interpersonal context, participants remain completely passive while they lay in the MRI scanner; they are subjected to the experimenter's criticism but cannot react. A behavioral measure that may reveal their emotional turmoil is absent.

An additional experimental approach for the interpersonal induction of anger is the classic social decision-making paradigm—the Ultimatum Game (UG) (Güth et al. 1982; Sanfey et al. 2003). In the UG, two players need to agree on how to split a sum of money between themselves in order to actually gain the money. One player makes an offer on how to split the sum, while the second decides whether to accept or reject the offer. Unequal offers of about 25 % and below the total sum are commonly rejected resulting in a monetary loss for both players. Such offers are regarded as unfair offers which violate social norms, elicit anger, and thus result in an aggressive retribution at one's own personal cost. Indeed, it was shown that anger mediated the relationship between the size of offers and rejection rates such that more anger resulted in increased rejections (Srivastava et al. 2009). Congruently, it was shown that unfair UG offers were associated with increased sympathetic arousal as measured by skin conductance response (SCR) (Van't Wout et al. 2006). A recent meta-analysis on the neural structures involved in processing

unfair offers compared to fair offers (Feng et al. 2015) found activity in the following regions: dACC, insula, ventrolateral, dorsolateral, and dorsomedial PFC, precuneus, temporal pole, temporalparietal junction (TPJ), and visual regions including the FFG. As detailed above, all these regions have previously been associated with various anger-related contexts.

Though consistent behavioral, psychophysiological, and neural evidence implicated anger with how people cope with unequal offers, it remains true that emotions are not the sole factor in explaining UG behavior (Civai 2013). Factors, such as reward valuation, fairness enforcement norms, and self-involvement, among others, may influence people's behavior in social decision-making paradigms (Rilling and Sanfey 2011). However, for the purpose of inducing anger and as long as such factors are being controlled for, it does not necessarily make a difference if one is angry because of the unfairness of an offer or by self-involvement as both are prerequisites for the subjective experience of anger. In addition to portraying an interpersonal situation, an additional benefit of the UG is that one can experimentally separate between the offer phase, which serves as the anger induction, and the decision-making phase. Thus, the behavior—a decision to accept or reject an offer—may serve as an objective measure of the associated emotional experience.

Indeed, additional evidence for the importance of the emotional response in driving behavior in the UG stems from emotion regulation studies which indicate that regulating anger may be important to the acceptance of unfair offers and that people who are better able to regulate anger associated with such offers are more likely to accept and financially benefit from them (Grecucci and Sanfey 2013). For example, explicitly instructing to use reappraisal to down-regulate emotions associated with unfair offers resulted in increased acceptance rates which were found to correlate with brain activity in an anterior region of the dlPFC (Grecucci et al. 2013). Furthermore, the insula showed effects of emotion modulation as activation decreased when down-regulating and increased when up-regulating. Additional studies on individual differences regarding the tendency to accept or reject unfair offers point at the involvement of ventral regions of the PFC. One such study revealed that activity in the vmPFC/OFC mediated the relationship between pre-UG testosterone levels and rejection rates (Mehta and Beer 2010). Nevertheless, there are several limitations when considering the UG as an anger-inducing paradigm. For one, the induction of anger is strictly focused on the amount of money offered. In addition, especially in the neuroimaging literature, the UG is implemented in a "single-shot" mode in which each offer is from a different, most often a virtual proposer, reducing to almost none the dynamic nature of the interaction. Angering situations, especially in bargaining contexts such as the UG, tend to spiral and escalate due to personal insults and provocations. The Denson and colleagues studies (2009, 2013) similarly lack this basic feature—subjects are provoked, but the naturalistic social-interactive and temporal dynamics of an angry experience is overlooked. A true engagement in social interaction occurs when people can communicate with others in their surroundings, adapting themselves contingently.

To try and tackle some of these limitations, a recent study (Gilam et al. 2015) created a modified version of the UG which incorporated, in a sense, the kind of provocation used by Denson and colleagues (2009, 2013). A repeated version of the UG in which participants decided to accept or reject offers from the same proposer was embedded with online verbal negotiations between the players after each round. Unbeknownst to the participants, the proposer was in fact a professional actor who used scripted and improvised provocations in concert with the sequence of mostly unfair offers to further induce interpersonal anger. All participants reported on anger as the dominant emotional experience, and importantly, anger reports increased as the interaction unfolded. In addition, the idiosyncratic tendencies to accept offers during this anger-infused social interaction, and thus gaining more money along the game, were associated with a balanced emotional profiled including both anger and positive emotions to an equal extent, as well as with increased activity in the anterior vmPFC/OFC and decreased activity in region of the brainstem possibly reflecting the Locus Coeruleus. It was also found that both vmPFC/OFC activity and functional connectivity between the insula and thalamus modulated the emotional experience en route to increased monetary gain. The fact that there were no control conditions, both for the anger induction provocations and for the social interaction, as the lack of clear instructions to regulate emotions, limit the capability to deduce whether these emotionally balanced participants were less angered or actually attenuated their angry response. And yet this paradigm seems to have mimicked realistically the dynamic features of an angry episode within the confined settings of the MRI scanner. A more general criticism, however, to such games as the UG is their excessive emphasis on decision-related processes and material payoffs, which are not a necessary part of real-life emotional experiences and social encounters. These flaws are important to further tweak and improve anger-inducing paradigms in future studies.

4 Concluding Remarks

The uniqueness of anger as an emotion is evident in that it is a negative emotion with a motivationally approach tendency. Furthermore, while anger is an emotion which seems to be apparent also in animals and features a bottom-up arousing component, in humans, anger has evolved into a complex multidimensional emotional construct, highly influenced by sociocultural contexts on the one hand and with profound personal and interpersonal ramifications on the other. Anger is thus inherently subject to and dependant on an individuals' ability to assert control and regulation over it. The wide distribution of brain regions as reviewed above may suggest that brain imaging studies thus far did not adequately dissect the complexity of the anger construct and did not distinguish between different modes of anger manifestation. Notwithstanding, the contextualized multidimensionality of anger may point toward the involvement of several neural circuits in mediating this psychobiological phenomenon. Indeed, there seems to be several findings that are

fairly consistent across most sets of neuroimaging studies. Thalamic, limbic, and brainstem regions seem to reflect threat detection network which has a critical role in reactive aggression (Siever 2008). Evidence is most strongly supported by animal models, though it seems a similar role for this network is apparent in humans, in which it is believed to be involved in mediating the experience of anger, especially by generating a state of arousal. Studies on human aggression have shown the involvement of these regions as well as of vmPFC/OFC and ACC. For example, it was recently shown that across participants, activity in the vmPFC while viewing an opponent bearing an angry facial expression compared to a neutral expression during an interactive competitive aggression task was negatively correlated with aggressive behavior (Beyer et al. 2014). In addition, within participants and specifically during the angry opponent trials, activity in the dACC was positively correlated with aggressive behavior. Yet, studying reactive aggression, even in social contexts, does not directly reflect the subjective experience of anger. Similarly, perceiving anger in faces or voices is not necessarily experiencing anger though such stimuli may serve as a social signal of threat. Interestingly though, it does seem that the same brain regions in the PFC are involved in the control and regulation of anger and aggression. Most notably, the vmPFC/OFC and lPFC (including IFG and dlPFC) have been associated with such regulatory functions; the former seems to be associated more specifically with regulation of anger experience and aggressive expressions of anger, while the latter with cognitive control of negative emotions in general (Buhle et al. 2014). The vmPFC/OFC has also been consistently associated with the expected subjective value of many different types of rewards, including monetary payoffs, snacks, and social rewards such as good reputation (Levy and Glimcher 2012). The vmPFC/OFC regulatory role may therefore reflect the expected value of the potential outcome of anger and aggression and thus direct behavior.

The reoccurrence of the insula and the dorsal aspect of the ACC might be related to their joint role in a network dedicated to detect salient sensory events, which has been associated with both physical and social pain (Iannetti and Mouraux 2010), both of which are primary antecedents of anger. A division of labor between these two highly interconnected regions has been suggested in which the insula is associated with the emotional experience, while the dACC is associated with allocation of control and modification of behavioral responses during challenging physical and cognitive situations (Gasquoine 2013). This suggested role of the dACC is congruent with its co-activation with regulatory regions of PFC during both anger and aggression paradigms. Finally, several regions associated with the mentalizing system such as the mPFC, PCC, temporal poles, and the TPJ (Denny et al. 2012) have also reappeared in various anger induction studies, whether self-generated or induced, albeit to a lesser extent. The involvement of this system seems to reflect the interpersonal nature of angering events, but the exact role of mentalizing in the experience, expression, and regulation of anger is still unclear. One important role may be that humans need to attribute the intention to do harm by another person in order to experience anger (Berkowitz and Harmon-Jones 2004). For example, it was shown that unfair UG offers randomly assigned by a computer

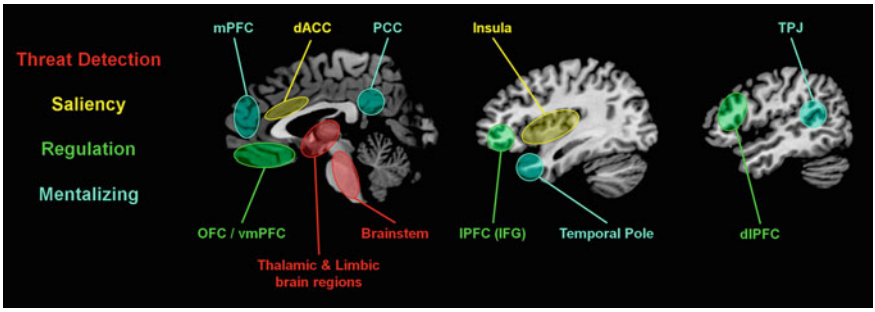

Fig. 1 Schematic scaffolding of the "angry brain." The MRI anatomical scans depict midsagittal (*left* Talairach slice $x = 3$), parasagittal (*middle* Talairach slice $x = 37$), and lateral (*right* Talairach slice $x = 47$) slices of the human brain. Four neural circuits seem to be involved in the subjective experience of anger: (1) threat detection, arousal, and reactive aggression (*red*) include thalamic (e.g., thalamus and hypothalamus), limbic (e.g., amygdala), and brainstem (e.g., PAG, locus coeruleus) regions; (2) saliency and perception of pain (*yellow*) include the insula and the dorsal anterior cingulate cortex (dACC); (3) emotion regulation (*green*) includes orbito-frontal cortex/ventromedial prefrontal cortex (OFC/vmPFC), lateral PFC (lPFC), most notably the inferior frontal gyrus (IFG), and dorsolateral PFC (dlPFC) regions; (4) mentalizing (*cyan*) includes medial PFC (mPFC), posterior cingulate cortex (PCC), temporal poles, and temporoparietal junction (TPJ) regions

were rejected less and also engaged less brain activity in bilateral anterior insula compared to similar offers allegedly made by a human counterpart (Sanfey et al. 2003). In a more specific case of an incidental transgression, mentalizing may have a role in understanding the accidental nature of the event and thus in fact serve as a regulatory mechanism in avoiding or reducing an angry reaction. The simplistic view would contend that mental state attribution is necessary for anger by the mere fact that anger is mostly experienced during social interactions, but this and other questions regarding the interaction between mentalizing and subjective anger deserve further scientific scrutiny.

In this review, we deconstructed human anger revealing its' physiological, cognitive, subjective, and behavioral components, portraying a socially contextualized regulated-prone multidimensional construct. However, most neuroimaging studies to date have focused on limited and specific aspects of the subjective experience of anger and therefore resulted in brain correlates dispersed across the entire brain. And yet, an overview of anger studies in the neuroimaging literature portrays several neural circuits that may provide the scaffolding for the reconstruction of the "angry brain" (Fig. 1). An important limitation to keep in mind regarding this review is that we focused solely on brain mapping techniques in healthy humans and did not integrate knowledge from other experimental modalities, such as electroencephalography or lesion studies, or various patient samples (for a review see Potegal and Stemmler 2010). We emphasize that to capture the large variety in the forms and fashions in which human anger is experienced and expressed and to portray the neurobehavioral substrates of these anger modes and related regulatory processes, studies in both healthy and patient populations must

embed realistic interpersonal situations within their paradigms. This reverberates with recent conceptual and empirical advances which emphasize the importance of creating an interactive social context when investigating the neurobiological underpinnings of emotional episodes (Gilam et al. 2015; Müller-Pinzler et al. 2015). An additional aspect of anger which seems to have missed the radar of neuroimaging studies is the necessity to explore the temporal unfolding of the emotional experience and its concomitant neural manifestation (Raz et al. 2012). The prevalence of dysregulated anger in a multitude of psychopathological conditions leads us to hope that future contributions of the neuroscience of anger may be useful not only to better understand this phenomenon but also to promote beneficial products such as improving anger management intervention programs.

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