The Interplay of Emotion and Cognition

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Until the 20th century, the study of emotion and cognition was largely a philosophical matter. Although contemporary theoretical perspectives on the mind and its disorders remain heavily influenced by the introspective measures that defined this earlier era of scholarship, the last several decades have witnessed the emergence of powerful new tools for objectively assaying emotion and brain function, which have yielded new insights into the interplay of emotion and cognition. Here, we consider ways in which this rapidly growing body of research begins to address more specific questions about how emotional and cognitive processes interact, how they are integrated in the brain, and the implications for understanding neuropsychiatric disease.

EMOTION INFLUENCES COGNITION

Emotion—including emotional cues, emotional states, and emotional traits—can profoundly influence key elements of cognition in both adaptive and maladaptive ways.

Emotional Stimuli Grab Attention

Emotionally-salient cues—snakes, spiders, angry faces, and erotica, to name a few—strongly influence attention. Attention is a fundamental property of perception and cognition. "Attention is necessary because…the environment presents far more perceptual information than can be effectively processed, one's memory contains more competing traces than can be recalled, and the available choices, tasks, or motor responses are far greater than one can handle" (Chun, Golomb, & Turk-Browne, 2011, p. 75). Attentional mechanisms select the most relevant sources of information while inhibiting or ignoring potential distractions and competing courses of action (Desimone & Duncan, 1995). Once a target is selected from competing options, attention determines how deeply it is processed, how quickly and accurately a response is executed, and how well it is later remembered.

Remarkably, emotion influences all of these processes. Across a range of tasks, emotionally-salient stimuli are more likely to be detected, to capture attention, and to be remembered (Carretie, 2014; Markovic, Anderson, & Todd, 2014). Emotional stimuli are associated with enhanced processing in

sensory regions of the brain and amplified processing is associated with faster and more accurate performance (Carretie, 2014; Kouider, Eger, Dolan, & Henson, 2009; Lim, Padmala, & Pessoa, 2009; Pourtois, Schettino, & Vuilleumier, 2013; Vuilleumier et al., 2002).

Individuals show marked differences in the amount of attention they allocate to emotionally salient information. Such attentional biases are intimately related to emotional traits and disorders. Hyper-vigilance for threat is a core component of both dispositional and pathological anxiety (Grupe & Nitschke, 2013). Children and adults with a more anxious disposition, like many patients with anxiety disorders, tend to allocate excess attention to threat-related cues when they are present in the environment, even when they are irrelevant to the task at hand (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van IJzendoorn, 2007; Dudeney, Sharpe, & Hunt, 2015; Okon-Singer, Alyagon, Kofman, Tzelgov, & Henik, 2011; Van Bockstaele et al., 2014). Anxious individuals are more likely to initially orient their gaze towards threat in free-viewing tasks; they are quicker to fixate threat-related targets in visual search tasks; and they show difficulty disengaging from threat-related distractors in spatial cueing, visual search, and dot-probe tasks (Armstrong & Olatunji, 2012; Aue & Okon-Singer, 2015; Cisler & Koster, 2010; Rudaizky, Basanovic, & MacLeod, 2014). In some cases, more complex patterns of initial vigilance followed by avoidance have been reported (Armstrong & Olatunji, 2012; Aue & Okon-Singer, 2015; Di Simplicio et al., 2014; Onnis, Dadds, & Bryant, 2011; Weierich, Treat, & Hollingworth, 2008; Zvielli, Bernstein, & Koster, 2014).

There is compelling evidence that attentional biases to threat causally contribute to the development and maintenance of extreme anxiety (Shackman, Kaplan, et al., *in press*). Attentional biases to threat can promote inflated estimates of threat intensity or likelihood (Aue & Okon-Singer, 2015), a key feature of the anxious phenotype (Grupe & Nitschke, 2013). Furthermore, interventions targeting the attentional bias to threat have been shown to reduce distress, behavioral signs of anxiety, and intrusive thoughts elicited during subsequent exposure to cognitive stressors, public speaking

challenges, and worry inductions in non-clinical samples (Dennis & O'Toole, 2014; MacLeod & Mathews, 2012). Consistent, medium-to-small treatment effects have also been found in clinical samples (Hakamata et al., 2010; Linetzky, Pergamin-Hight, Pine, & Bar-Haim, 2015; MacLeod & Clarke, 2015).

The impact of emotion on attention reflects the coordinated activity of multiple cortical and subcortical brain regions (Arend, Henik, & Okon-Singer, 2015; Pessoa & Adolphs, 2010). Here, we focus on the role of the amygdala, a heterogeneous collection of nuclei buried beneath the temporal lobe (Fox & Kalin, 2014; Freese & Amaral, 2009). Imaging and single unit studies performed in humans and monkeys demonstrate that the amygdala is sensitive to a broad range of emotionally and motivationally significant stimuli, including emotional faces and images, erotica, food, and substance cues (Chase, Eickhoff, Laird, & Hogarth, 2011; Costafreda, Brammer, David, & Fu, 2008; Fried, MacDonald, & Wilson, 1997; Fusar-Poli et al., 2009; Gothard, Battaglia, Erickson, Spitler, & Amaral, 2007; Hoffman, Gothard, Schmid, & Logothetis, 2007; Kirby & Robinson, *in press;* Kuhn & Gallinat, 2011; Lindquist, Wager, Kober, Bliss-Moreau, & Barrett, 2012; Sabatinelli et al., 2011; Sergerie, Chochol, & Armony, 2008; Sescousse, Caldu, Segura, & Dreher, 2013; Tang, Fellows, Small, & Dagher, 2012; Wang et al., 2014). Mechanistic studies in animals and anatomical tracing studies in nonhuman primates suggest that the amygdala can prioritize the processing of emotional stimuli via at least two mechanisms: directly, via excitatory projections to relevant areas of sensory cortex (e.g., fusiform face area) and indirectly, via projections to ascending neurotransmitter systems in the basal forebrain and brainstem that, in turn, modulate sensory cortex (i.e., increase the neuronal signal-to-noise ratio; Davis & Whalen, 2001; Freese & Amaral, 2009). Imaging research shows that variation in amygdala activation predicts whether degraded emotional stimuli are detected and that this association with performance is mediated by enhanced activation in sensory cortex (Lim et al., 2009). Manipulations that increase amygdala reactivity also enhance behavioral measures of threat vigilance (Herry et al., 2007). Conversely, disorders (e.g., autism) and manipulations that reduce the amount of attention

allocated to aversive or potentially threat-relevant information lead to decreased amygdala engagement (Dalton et al., 2005; Pessoa, McKenna, Gutierrez, & Ungerleider, 2002; Urry, 2010; van Reekum et al., 2007). Likewise, patients with amygdala damage and monkeys with selective amygdala lesions fail to show enhanced activation to emotional cues in sensory cortex, indicating that the amygdala mechanistically contributes to the attention-grabbing properties of emotional stimuli (Hadj-Bouziane et al., 2012; Rotshtein et al., 2010; Vuilleumier, Richardson, Armony, Driver, & Dolan, 2004).

The amygdala is not a passive recipient of emotional information in the environment. In addition to boosting sustained attention and vigilance, the amygdala plays a key role in redirecting gaze (i.e., overt attention) to the most emotionally salient features of facial expressions (Shackman, Kaplan, et al., *in press*). Using a combination of eye tracking and brain imaging, we have demonstrated that humans are biased to reflexively attend the eye region of the face, that this bias is most pronounced for fearful faces, and that individuals showing greater amygdala activation are more likely to shift their gaze to the eyes (Gamer & Buchel, 2009; Scheller, Buchel, & Gamer, 2012). This bias appears to be exaggerated among individuals with a more anxious, neurotic disposition (Perlman et al., 2009). Importantly, individuals with damage to amygdala do not show reflexive saccades to the eyes (Gamer, Schmitz, Tittgemeyer, & Schilbach, 2013). This observation is consistent with evidence that patient SM, who is characterized by near-complete, bilateral destruction of the amygdala, fixates the mouth rather than the eyes in both real-world social interactions and well-controlled laboratory assessments (Adolphs et al., 2005; Spezio, Huang, Castelli, & Adolphs, 2007). Collectively, these observations indicate that the amygdala is crucial for the rapid detection and reorienting of attention to emotionally and motivationally significant cues.

Emotional Cues Hijack Working Memory Capacity

Selective attention is tightly linked with working memory (Ikkai & Curtis, 2011). Working memory is the 'blackboard of the mind' (Goldman-Rakic, 1996), a limited-capacity workspace where information

is actively maintained, recalled, and manipulated (D'Esposito & Postle, 2015). The transient representation of task-sets, goals, and other kinds of information in working memory plays a crucial role in sustaining goal-directed attention, biasing behavior in the face of distraction, and regulating emotion (Miller & Cohen, 2001). In short, information transiently held in working memory is a key determinant of our momentary thoughts, feelings, and behavior.

Recent work by our group indicates that emotionally salient information enjoys privileged access to working memory. Using a combination of electrophysiological and behavioral assays, we showed that threat-related distracters infiltrate working memory and that this effect is exaggerated among individuals with a more anxious disposition (Stout, Shackman, Johnson, & Larson, 2014; Stout, Shackman, & Larson, 2013). In other words, anxious individuals allocate excess storage capacity to threat, even when it is completely irrelevant to the task at hand and no longer present in the external world. This may help to explain anxious individuals' tendency to experience heightened distress in the absence of clear and immediate danger (Davis, Walker, Miles, & Grillon, 2010; Grupe & Nitschke, 2013; Shackman, Stockbridge, LeMay, & Fox, *in press*). Once lodged in working memory, threat-related information is poised to bias the stream of information processing (i.e., attention, memory retrieval, and action) long after it is no longer present in the real world, promoting worry and other maladaptive cognitions (Thiruchselvam, Hajcak, & Gross, 2012). Consistent with this hypothesis, recent work suggests that interventions aimed at strengthening working memory can cause lasting reductions in anxiety (Sari, Koster, Pourtois, & Derakshan, *in press*).

Emotional States Strengthen Some Cognitive Processes While Weakening Others

Classically, cognition and emotion have been viewed as oppositional forces (Shackman, Fox, & Seminowicz, 2015). From this perspective, moods and other emotional states simply short-circuit cognition. But with the ascent of evolutionary theory in the 19th century, many scientists adopted the view that emotions are functional and enhance fitness (Darwin, 1872/2009; Schwabe & Wolf, 2013;

Todd & Anderson, 2013). In short, emotions are more adaptive than not and "there is typically more cooperation than strife" between emotion and cognition (Levenson, 1994). Consistent with this more nuanced perspective, there is growing evidence that experimentally elicited states of stress and anxiety facilitate some kinds of information processing, while degrading others. For example, anxiety enhances sustained attention and vigilance, potentiating early sensory cortical responses to innocuous environmental stimuli and increasing the likelihood that emotionally-salient information will be detected (Shackman, Maxwell, McMenamin, Greischar, & Davidson, 2011). Other work indicates that stress and anxiety disrupt working memory, particularly visuospatial working memory (Arnsten, 2009; Arnsten & Goldman-Rakic, 1998; Robinson, Vytal, Cornwell, & Grillon, 2013; Shackman et al., 2006).

Recent work suggests that some of these consequences may reflect stress-induced sensitization of the amygdala. Brief exposure to acute stressors (e.g., threat-of-shock, aversive film clips) potentiates defensive reactions elicited by threat-related facial expressions (Grillon & Charney, 2011), promotes sustained increases in spontaneous amygdala activity (Cousijn et al., 2010), and amplifies amygdala reactivity to threat-related faces (Pichon, Miendlarzewska, Eryilmaz, & Vuilleumier, 2015; van Marle, Hermans, Qin, & Fernandez, 2009). Acute stressors produce even longer-lasting changes (minutes to hours) in the functional connectivity of the amygdala (Vaisvaser et al., 2013; van Marle, Hermans, Qin, & Fernandez, 2010). Stress-induced sensitization appears to be elevated in individuals with a more anxious, neurotic disposition (Everaerd, Klumpers, van Wingen, Tendolkar, & Fernandez, 2015).

COGNITION REGULATES EMOTION

In the first edition of *The Nature of Emotion*, Ekman and Davidson wondered whether we can control our emotions. Two decades later, there is ample affirmative evidence. In fact, humans frequently regulate their emotions and we do so using a variety of increasingly well understood cognitive strategies (Gross, 2015a, 2015b; Sheppes, Suri, & Gross, 2015). Work to understand the

neurobiological underpinnings of this core human capacity indicates that circuits involved in attention and working memory play a crucial role in the regulation of emotion and other, closely related aspects of motivated behavior, such as temptation and craving (Etkin, Buchel, & Gross, 2015; Hare, Malmaud, & Rangel, 2011; Kelley, Wagner, & Heatherton, 2015).

Perhaps the most basic strategy for reducing distress is attentional avoidance; that is, simply shift attention look away from the source of distress (Gross, 2015a). Covert or overt attentional redeployment is a potent, relatively effortless means of regulating the engagement of subcortical structures, such as the amygdala, that play a key role in orchestrating emotional states (Dalton et al., 2005; Okon-Singer, Lichtenstein-Vidne, & Cohen, 2013; Okon-Singer, Tzelgov, & Henik, 2007; Pessoa et al., 2002; Urry, 2010; van Reekum et al., 2007).

Other strategies for regulating emotional states, such as cognitive reframing and reappraisal (e.g., Heller et al., 2009), require the effortful maintenance of an explicit regulatory goal or model and depend on a working memory circuit encompassing the lateral prefrontal (PFC) and posterior parietal cortices (PPC) (Buhle et al., 2014; Rolls, 2013). Consistent with this perspective, individual differences in working memory capacity are predictive of reappraisal success (Etkin et al., 2015) and experimentally elicited stress, which is known to degrade working memory, disrupts the regulation of aversive emotional states (Raio, Orederu, Palazzolo, Shurick, & Phelps, 2013). Moreover, recent work using transcranial direct-current stimulation demonstrates that the lateral PFC is crucial for emotion regulation (Feeser, Prehn, Kazzer, Mungee, & Bajbouj, 2014), consistent with work focused on the neurobiology of impulsivity and self-control (Wagner & Heatherton, 2014).

EMOTION AND COGNITION ARE FUNCTIONALLY AND ANATOMICALLY INTEGRATED

Humans tend to experience cognition and emotion as fundamentally different. Emotion is infused with feelings of pleasure or pain and manifests in readily discerned changes in the body, whereas cognition

often appears devoid of substantial hedonic, motivational, or somatic features. These apparent differences in phenomenological experience and peripheral physiology led many classical scholars to treat emotion and cognition as distinct mental faculties (Okon-Singer, Hendler, Pessoa, & Shackman, 2015).

But contemporary theorists have increasingly rejected the claim that emotion and cognition are categorically different (Barrett & Satpute, 2013; Damasio, 2005; Lindquist & Barrett, 2012; Pessoa, 2013). This perspective reflects four lines of evidence. First, imaging research demonstrates that key emotional and cognitive processes are co-localized in the brain (Shackman, Salomons, et al., 2011). Second, electrophysiological research shows that prototypical cognitive control signals (e.g. No-Go N2, error-related negativity) systematically co-vary with emotional traits and states (Cavanagh & Shackman, 2015). Third, canonical territories of 'the cognitive brain' (e.g., lateral PFC) play a central role in regulating emotion and motivated behavior (Buhle et al., 2014). Fourth, canonical territories of 'the emotional' brain (e.g., amygdala) regulate cognition via their influence over the brainstem neurotransmitter systems (Arnsten, 2009; Davis & Whalen, 2001). In this way, the amygdala can transiently assume control over attention, working memory, and behavior in situations that favor immediate responses over slower, more deliberate forms of reasoning. Of course, this can be maladaptive and there is abundant evidence that stress promotes impulsive, risky behaviors (Kelley et al., 2015; Wagner & Heatherton, 2014) and disrupts volitional forms of emotion regulation (Raio et al., 2013).

CONCLUSIONS

The last decade has witnessed an explosion of interest in the interplay of emotion and cognition and greater attention to key methodological and inferential pitfalls (Shackman et al., 2015; Shackman et al., 2006). The work we have highlighted illustrates the tremendous advances that have already been made. This body of research demonstrates that emotional cues, states, traits, and disorders can

profoundly influence key elements of cognition, including selective attention, working memory, and cognitive control. In turn, circuits involved in attention and working memory contribute to the regulation of emotion. The distinction between 'the emotional brain' and 'the cognitive brain' is blurry and context-dependent. Indeed, there is compelling evidence that territories (e.g., dlPFC, MCC) and processes (e.g., attention, working memory, cognitive control) conventionally associated with cognition play a central role in emotional states, traits, and disorders. Furthermore, putatively emotional and cognitive regions dynamically influence one another via a complex web of recurrent, often indirect anatomical connections in ways that jointly contribute to adaptive behavior. These observations show that emotion and cognition are deeply interwoven in the fabric of the brain, suggesting that widely held beliefs about the key constituents of 'the emotional brain' or 'the cognitive brain' are fundamentally flawed.

Despite this progress, our understanding of the interplay of emotion and cognition remains far from complete and a number of important challenges remain. Indeed, we are reminded of Ekman and Davidson's comment in the first edition of *The Nature of Emotion*: "There are many promising findings, many more leads, [and] a variety of theoretical stances" (Ekman & Davidson, 1994). As described in detail elsewhere, addressing these challenges will require a greater emphasis on: (a) assessing the real-world relevance of laboratory assays, including measures of brain activity; (b) characterizing the distributed circuits underlying emotion-cognition interactions, and (c) integrating mechanistic and non-mechanistic research strategies (Okon-Singer et al., 2015; Shackman et al., 2015).

Developing a deeper understanding of the interplay of emotion and cognition is a matter of theoretical as well as practical importance. Many of the most common, costly, and challenging to treat neuropsychiatric disorders—anxiety, depression, schizophrenia, substance abuse, chronic pain, autism, and so on—involve prominent disturbances of both cognition and emotion, suggesting that

they can be conceptualized as disorders of the emotional-cognitive brain. These disorders impose a larger burden on public health and the global economy than either cancer or cardiovascular disease (Collins et al., 2011; DiLuca & Olesen, 2014; Whiteford et al., 2013), underscoring the need to accelerate efforts to understand the mechanisms underlying the interplay and integration of emotion and cognition.

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