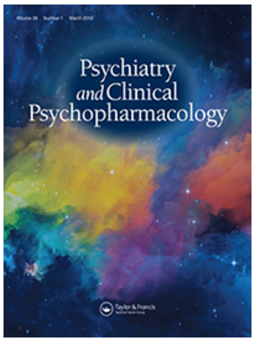

Psychiatry and Clinical Psychopharmacology

ISSN: 2475-0573 (Print) 2475-0581 (Online) Journal homepage: https://www.tandfonline.com/loi/tbcp21

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To cite this article: Sezin Öner (2018) Neural substrates of cognitive emotion regulation: a brief review, Psychiatry and Clinical Psychopharmacology, 28:1, 91-96, DOI: 10.1080/24750573.2017.1407563

To link to this article: https://doi.org/10.1080/24750573.2017.1407563

Published online: 28 Nov 2017.

PSYCHIATRY AND CLINICAL PSYCHOPHARMACOLOGY, 2018
VOL. 28, NO. 1, 91–96
https://doi.org/10.1080/24750573.2017.1407563

REVIEW ARTICLE

OPEN ACCESS

Neural substrates of cognitive emotion regulation: a brief review

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ABSTRACT
The current paper aims to review the recent evidence on the neural correlates of emotion regulation. The review is organized into two main sections. First, cognitive models that neuroimaging research is based on are introduced with a specific emphasis on the process-specific explanations of emotion regulation. In the second section, neuroimaging research is discussed in line with the evidence from human and nonhuman animals. Existing evidence suggests that regulation of emotions may be achieved either by bottom-up, subcortical, or top-down frontal mechanisms. The former way acts on the initial phases of emotion generation, whereas the latter appears to influence the higher-order structures for cognitive change and modulation of emotional responses. Although there is still an ongoing debate on when the generation stops and regulation starts on the emotion process, with respect to neural mechanisms, underlying regulatory strategies appear to be more consistent. Potential questions are also addressed for future research to contribute to especially the individual differences adaptive emotion regulation.

ARTICLE HISTORY
Received 1 November 2017
Accepted 17 November 2017

KEYWORDS
Emotion regulation; neuroimaging research; cognitive reappraisal; suppression; cognitive control

There has been growing interest in the concept of emotion regulation especially over the past two decades. Intensive empirical research advanced our knowledge regarding the developmental, socio-cognitive, neuroscientific, and clinical implications of emotion regulation. On one hand, the field has become a hot topic integrating different areas of psychology, on the other hand, alternative conceptualizations of emotion, as well as its regulation, have been proposed, which has raised important debates in the scientific study of emotion regulation [1–3].

Emotion regulation has been defined as a range of processes by which individuals alter the onset, course, or experience of their emotions [4]. Regulatory processes may be explicit, with conscious awareness [5] or implicit, rather operating automatically [6]. Although the common sense conception of regulation has focused on decreasing negative affect, regulation may target the maintenance, increase, or decrease negative or positive affect [7] via either covert or overt processes [8]. In addition, emotions may be self-regulated, as called intrinsic regulation, or may be supported external environment (i.e. significant others, environmental cues) [9]. Therefore, there have been multiple routes and sources for regulation of emotions, all of which modifies at least one aspect of emotion such as physiology, attention, appraisals, experience, and expression [10,11].

Current review focuses on the neural correlates of cognitive regulation of emotion. First, theoretical assumptions underlying the cognitive account are summarized, which was then followed by the review of the neuroimaging research conducted with human and nonhuman animals.

Cognitive accounts of emotion regulation

Process-specific explanation [1,10] has been one of the prominent accounts of emotion regulation. The model suggested that it was suggested that emotion generation process involves the encounter with a real or imagined stimulus. Once after the individual attends to it, a subjective meaning is attached (primary appraisal). The cognitive evaluation of the organism then triggers an emotional response, physiological, behavioural, or experiential. Since emotions come into being and are manifested in increasing intensity as the time unfolds, regulation at later stages of the emotional process requires more effortful control. Regulation may occur at any level through the emotion generation. Regulation attempts may target the context or the emotion-generating situation (situation selection) or may act on the situational demands (situation modification) [10].

The role of cognitive resources becomes more salient once after the emotional context becomes solid. Individuals may modify the attention devoted to the emotionally evocative stimulus. For example, when you are watching a horror film, you may mentally or visually distract yourself and receive less input to be

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regulated [10]. An alternative way of distraction involves replacing the disturbing with more neutral or positive ones. Despite the difference in the main target (i.e. distract from the primary negative emotion vs. attend to the more positive), both forms of disengagement have been found effective in reducing the emotional experience [12,13].

Regulation may occur at the level of appraisal as well. Cognitive reappraisal represents the further mental elaborations that result in a change in the initial meaning of the emotional stimuli. Since reappraisal is implemented later in the emotion-generative process, it requires certain extent of emotional processing, but still, it has been demonstrated as the most effective forms of regulation in terms of decreasing physiological activation and subjective experience of negative emotions [13–15] and increasing positive affect in daily life [7].

If emotions are not regulated even at the reappraisal phase, response-modulation strategies may be implemented [10,16]. Expressive suppression, the most studied strategy, aims to conceal the overt expression of emotion. However, regulation at this point is harder since emotional tendencies are fully activated until they progressed to this stage as being unregulated. Accordingly, suppression has been demonstrated to be an inefficient and costly emotion regulation strategy, taxing various areas of psychological functioning, such as memory impairments [17], heightened autonomic arousal [10,18] and rebounds of suppressed material [19].

The basic premise within this model is that, later the emotion regulatory processes occur, it will not only require more effort to regulate but also it is more likely that intensity of the emotion will interfere with the regulation efforts [20]. Regulation successes, therefore, depends on whether regulation is executed at an earlier or later stage, suggesting that if individuals timely make use of regulatory resources, then even highly intense emotion can be regulated efficiently. More specifically, since attentional mechanisms operate earlier, they prevent the emotional information from entering into working memory [21], which leaves no need to act on the cognitive appraisals associated with the stimuli.

Neurobiology of emotion regulation

Research on the neural bases of emotion regulation has made substantial progress over the past decade [22]. Although studies with nonhuman animals have provided valuable insight to formulate basic models of emotion regulation, technical developments for imaging human brain allowed to further examine the higher-order neural processes underlying in emotion regulation. Further cross-species translational work provided a comparative approach, demonstrating the similarities and distinctions of human affective system form nonhuman animals. This section is organized under two main headlines, one includes theoretical perspectives and evidence on emotions in nonhumans and the other section targets mostly human studies focusing on the effectiveness of emotion regulation.

Basic emotions in the brain: nonhuman research

The basic premise of the basic emotions theory is that certain emotions are hardwired in the brain and each of them operates with a unique mechanism across species [23,24]. The so-called affect programme that each emotion is associated with involves brain circuits, coordinated emotional experiences, response tendencies, and behavioural and physiological expressions dedicated to that unique emotion. Considering the evolutionary origins of the limbic system, Panksepp [25] argued that direct stimulation of neural regions best representing these emotion mechanisms triggers the specific affect programme, which allows one to capture the pure form of basic emotions. In line with his argument, studies with direct brain stimulation [26,27] have been demonstrated that certain evolutionarily conditioned basic emotions (i.e. fear, anger) could be generated via functions of subcortical brain regions of amygdala and periaqueductal grey matter. Although these studies informed us about the emotion-generative processes, it does not tell much about the regulatory processes.

The role of amygdala in emotion regulation, as distinct from emotion generation, has been demonstrated in subsequent research. In a typical classical conditioning paradigm, Amorapanth and colleagues [28] trained rats to freeze in response to conditioned stimulus (emotional behaviour), but when trained, they could learn strategies to terminate or prevent the delivery of the conditioned stimulus (regulatory behaviour). However, it was found that damage to the central amygdala impaired emotional behaviour (freezing), whereas the ability to learn how to terminate or prevent the shocks remained intact. On the other hand, damage to the basal amygdala resulted in the opposite pattern of impairment such that although animals showed appropriate emotional behaviour, they could not learn how to manage the shocks, suggesting for a neural dissociation in the generation and regulation of emotional behaviour.

Modulating functions of cortical networks have been indicated in classical conditioning and instrumental conditioning paradigms [29]. The findings were in general consistent that reversal of stimulus-reward associations [30], instrumental avoidance of aversive experiences, and classical conditioning of fear responses have been found to rely on the similar the neural pathway linking nucleus accumbens, ventral prefrontal cortex, orbitofrontal cortex (OFC), and anterior cingulate (ACC). What is common to these learning mechanisms is that, as the emotional value of a stimulus is modified, the organism is expected to replace the existing, more automatic responses so as to match the newly acquired stimulus value. Regulation of emotional responses in this way has been implicated as bottom-up appraisal processes, which are further explained below.

Top-down control of emotions: human research

Although bottom-up and top-down regulation of emotions were not such distinct to be associated with nonhumans versus humans, higher-order cortical functions observed in studies with humans were rarely indicated in the animal work [5]. Therefore, current evidence with humans provided much more than the identification of the basic bottom-up processes and contributed to the integration of low-level and high-level neural functions.

Top-down processes have been emphasized by appraisal theories of emotional regulation. Once, a subjective meaning is attached to the emotional stimulus, whether it is threatening, rewarding, or instrumental with goal states, the organism evaluates the circumstances, and puts forward automatic or effortful regulatory behaviours in line with the expectations, goals, or needs [10,31].

On the other hand, appraisal theories acknowledge that although appraisals could be generated automatically, they are not necessarily built upon specific stimulus-response linkages, but rather can be modulated depending on the individual's learning history, personality, and the context in general [1,31]. In that sense, top-down processes represent more active control over the emotional experience, as well as the regulation and particularly different from the basic emotion approach [25] appraisal theories emphasize the more flexible operations of bottom-up processes in the cognitive regulation of emotion.

Along with the theoretical assumptions, higher-order frontal structures have been implicated in the effortful control of emotions along with deactivation of subcortical regions (i.e. amygdala) associated with emotional experience [32–34]. Modulation of attentional processes was found to be associated with increased activity in the dorsolateral prefrontal cortex (DLPFC), the medial frontal cortex (MFC), the ACC, and the OFC, which was accompanied by decreased activity in subcortical affect mechanisms. However, since these studies, in general, involved an alternative distractive task, other than the emotional one, it is also possible that prefrontal activity may be reflecting the individual's attempts to perform adequately on the alternative task.

Regarding cognitive reappraisal, consistent evidence demonstrated that the dorsal ACC and the prefrontal regions that are involved in working memory [5,33–35] as well as the linguistic and long-term memory processes have been implicated in the cognitive change mechanisms [36,37]. In addition, top-down regulation of reappraisal attenuates activity in subcortical regions. As Ochsner and colleagues [37] demonstrated successful reappraisal was associated with decreased amygdala activity accompanied by the increased middle frontal gyrus (MFG) activity. Regarding this, it was argued that although the MFG and the amygdala were not linked directly, the MFG has direct projections to the medial prefrontal cortex (MPFC) regions that modulate amygdala. Similar neural activity, with an additional increase in the ventromedial prefrontal cortex, was found in extinction learning, indicating that cognitive strategies to regulate emotions as in reappraisal and extinction learning are supported by similar neural mechanisms [38].

Neural processes underlying reappraisal have been expanded considering different regulatory goals. In a recent study, Holland and Kensinger [39] asked participants to recall autobiographical memories in response to negative and neutral cue words about one week before the functional magnetic resonance imaging scan. During the scanning, they were given the cue words and asked to recall the previously reported memories while either up-regulating, down-regulating, or maintaining the emotional intensity associated with the experience. It was found that when down-regulation emotions, greatest activation was observed during memory onset in dorsal (DLPFC), ventrolateral (VLPFC), and medial (MPFC) regions of the prefrontal cortex (PFC), which was accompanied by decreased activity in the hippocampal regions and amygdala. Down-regulation of negative affect occurred early in the process (at the memory onset), before the emotional experience fully unfolded and became more intense. Up-regulation of emotions were engaged in similar frontal and temporal regions while the down-regulation were engaged in subcortical regions in reverse patterns. However, the frontal activity was greater during instruction and elaboration compared to memory onset. The findings are noteworthy such that although reappraisal recruited similar neural regions, the time course of activation differed depending on the target goal, either to up-regulate or down-regulate. Also, in line with the process model [11,12], as many features of the emotion get activated, emotional intensity increased, requiring more elaboration in order to be regulated. Therefore, it is very likely that neural circuits underlying cognitive reappraisal are not only functionally distinct but also their relative involvement may differ over the course of the regulation.

Relative contribution of different brain region over the course of the regulation was investigated in a recent meta-analysis. Kohn and colleagues [40] examined the activation likelihood estimates of core neural circuits involved in reappraisal and then integrated their findings with the Gross's [1,10] process model of emotion regulation. In their heuristic model, emotion regulation was explained in three major stages. Subcortical brain structures of the amygdala and the ventral striatum are involved in the transmission of the emotional arousal to the VLPFC, anterior insula, and as well as to angular gyrus in the first stage. Then, affective evaluation starts; the VLPFC decides whether the emotional arousal needs to be regulated based on the motivational or contextual demands and conveys the decision to the DLPFC. Therefore, the DLPFC processes the information received from the VLPFC and initiates emotion regulation in the second stage. Emotion regulation is executed in the third stage in which the DLPFC, directly or indirect via anterior midcingulate cortex, projects to angular gyrus, supplementary motor area, amygdala and ventral striatum, creating the regulated emotion with associated physiological, motor responses.

The heuristic model [40] has been informative not only theoretically but also in terms of the methodology utilized to extract the relative involvement of regulatory regions. Correspondence of the model predictions with previous research, such as, functional dissociation between the DLPFC and the VLPFC for stimulus control and stimulus evaluation, respectively, has been demonstrated in several studies [41,42]. In addition, further studies testing the model may inform about the neural mechanisms involved in different reappraisal strategies (i.e. self-distancing vs. challenging [43]), which would presumably contribute to our knowledge for regulation success, and as well as interventions for clinical populations.

Clinical implications of emotion regulation

Clinical accounts of emotion regulation have dated back to theorization on psychological defenses [44], coping [45], and attachment [46]. As the goal of emotion regulation is to intervene the emotion generation (i.e. the onset, course) or responses to emotions (i.e. behaviour, subjective experience), dysfunctional emotional regulation has been operationalized as the failure of regulation when emotional distress exceeds the individual's capacity to effortfully implement appropriate strategy [47].

Difficulties in the experience and regulation of emotion characterize the primary source of discomfort in almost all classes of psychopathology [48]. For anxiety and mood disorders, dysfunctional emotion processes constitute the core features of the psychopathology, whereas in substance abuse and eating disorders, emotion dysregulation is so pervasive in the individual's life that consequences of regulation deficits appear directly as the symptoms (i.e. difficulties in inhibition of urges) [49].

However, it is even more problematic in clinical samples to identify when does emotion regulation become dysfunctional. Emotion regulation processes may be interrupted due to difficulties in the early emotion-generation phase. Automatic inhibition of the primary emotion leads to generation of a secondary emotional response. For example, in individuals with borderline personality disorder, frustration may be transformed in the initial phases of in the emotion generation and expressed as anger [50]. Experience of frustration is blocked but this emotional suppression does not occur at the level of response but rather, the secondary emotion is activated and replaces the genuine emotion, which then becomes the main trigger of another emotion-generative phase [51]. Such an emotional replacement is associated with an emotional hypoawareness [48] because, not only the primary genuine emotional experience is blocked, but also the individual guided by the artificial secondary emotion and, therefore, the motivational-informational value of the emotion will no longer help the individual resolve the source of the distress [52].

Emotional hyperawareness may have problematic consequences as well. Enhanced attention of bodily cues as in the panic disorder [53] modulate the phase of emotion generation and even in the absence of an actual threat, leads the individual to experience substantial anxiety as if there exists a real threat. Such a hypervigilance captures the attention and further interrupts the implementation of effective regulation strategies.

On the other hand, it is also possible that emotional difficulties may result from the inflexible use of regulation strategies [54,55]. When individuals are unable to replace the habitual regulatory strategies that are no longer adaptive, individuals tend to experience a mismatch between strategies utilized and contextual demands and diverge from their current goals [48]. For example, in cases of pathological anxiety, individuals attempt to regulate their anxiety by experiential avoidance, which constricts their behavioural repertoire and prevents the individual to encounter with the anxiety-provoking target. Even when they expose themselves to anxiety to provoking situations, use of safety behaviours prevents them to receive experiential feedback and counteract maladaptive behaviour patterns [47,56].

Overall, a vast number of studies have addressed the emotional problems because of their high prevalence in clinical samples. Some of these emotional problems may be the result of the emotion generation, rather than the regulation process. Difficulties in regulation, however, emerge as a function of not only the selection and implementation of the maladaptive strategies, but also failure to monitor the efficacy of these strategies. Accordingly, recent studies [48,55] put more effort to characterize the clinical problems associated with specific regulatory impairments, which encourages further work for clinical profiling to develop more specific interventions targeting difficulties in emotion regulation.

Conclusion

Overall, basic emotion approach distinguished regulation of emotion from the emotion itself, each of which is represented in unique brain circuits whereas, for appraisal theories, emotion generation and emotion regulation occur on a continuum and neural circuits devoted to the experience and regulation of emotions may vary depending on the appraisal. Despite slight differences in the theoretical propositions, both views consider emotional states as distinct mental representations having unique elements. What evidence from the neuroimaging research suggests that, first, basic, bottom-up and higher-order, top-down processes may utilize different neural mechanisms, but both of them contribute to the generation of emotional responses. Second, neural processes of regulation vary as a function of the particular strategy utilized. Third, emotional intensity associated regulatory goals are likely to influence the timing of emotion regulation.

Although considerable progress has been made, there is much to do in the field of emotion regulation. Regulation attempts and regulation success are more clearly determined and tested for the neural predictors underlying more efficient regulation. Behavioural and neural evidence especially from clinical samples may broaden our understanding with respect to the emotion regulation difficulties associated with various forms of psychopathology. Another line of research should address automatic, implicit emotion regulation strategies and determine whether similar neural regions are involved as in the implementation of effortful strategies. Particularly, these two questions have the guiding potential for future research and I believe, have substantial contribution to the current knowledge.

Disclosure statement

No potential conflict of interest was reported by the authors.

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