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Neuroimaging cognitive reappraisal in clinical populations to define neural targets for enhancing emotion regulation. A systematic review

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ABSTRACT

Reduced capacity to cognitively regulate emotional responses is a common impairment across major neuropsychiatric disorders. Brain systems supporting one such strategy, cognitive reappraisal of emotion, have been investigated extensively in the healthy population, a research focus that has led to influential meta-analyses and literature reviews. However, the emerging literature on neural substrates underlying cognitive reappraisal in clinical populations is yet to be systematically reviewed. Therefore, the goal of the current review was to summarize the literature on cognitive reappraisal and highlight common and distinct neural correlates of impaired emotion regulation in clinical populations. We performed a two-stage systematic literature search, selecting 32 studies on cognitive reappraisal in individuals with mood disorders (n = 12), anxiety disorders (n = 14), addiction (n = 2), schizophrenia (n = 2), and personality disorders (n = 5). Comparing findings across these disorders allowed us to determine underlying mechanisms that were either disorder-specific or common across disorders. Results showed that across clinical populations, individuals consistently demonstrated reduced recruitment of the ventrolateral prefrontal cortex (vlPFC) and dorsolateral prefrontal cortex (dlPFC) during downregulation of negative emotion, indicating that there may be a core deficit in selection, manipulation and inhibition during reappraisal. Further, in individuals with mood disorders, amygdala responses were enhanced during downregulation of emotion, suggesting hyperactive bottom-up responses or reduced modulatory capacity. In individuals with anxiety disorders, however, emotion regulation revealed reduced activity in the dorsal anterior cingulate cortex (dACC) and inferior/superior parietal cortex, possibly indicating a deficit in allocation of attention. The reviewed studies thus provide evidence for both disorder-specific and common deficits across clinical populations. These findings highlight the role of distinct neural substrates as targets for developing/assessing novel therapeutic approaches that are geared towards cognitive regulation of emotion, as well as the importance of transdiagnostic research to identify both disorder specific and core mechanisms.

Introduction

The combined lifetime prevalence of anxiety, mood, externalizing and substance use disorders is estimated to be 18–36% worldwide (Kessler et al., 2009). These neuropsychiatric disorders pose a substantial economic burden to the society and significant personal distress to the affected individuals and their families. A recent comprehensive meta-analysis of mortality rates indicates that mental health disorders lead to 8 million deaths annually worldwide (Walker et al., 2015), with staggering short- and long-term societal costs for healthcare expenditures and impaired functioning (Kessler et al., 2009).

Across these major neuropsychiatric disorders a common cognitive impairment is a reduced capacity for emotion regulation. Persistent negative appraisal is thought to play a key role in the initiation and maintenance of depressed mood (Beck et al., 1979) and the maintenance of excessive anxiety (Amstadter, 2008) and to contribute to psychosis (Livingstone et al., 2009). Moreover, the loss of control over drug intake in addiction has been linked to a compromised regulation of drug wanting (Goldstein and Volkow, 2011). A reduced capacity for cognitive regulation of emotion is assumed to arise from both sensitized emotional/reward brain systems and weakened brain networks for cognitive control (Etkin and Wager, 2007; Goldstein and Volkow, 2011; Hamilton et al., 2012). However, while there is mounting evidence implicating these brain systems during symptom provocation and performance of cognitive tasks in general, the literature on the functional neuroimaging studies that investigate

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emotion regulation per se has not been reviewed across these clinical populations.

As the effective use of emotion regulation strategies has been shown to constitute a resilience factor for mental health (Min et al., 2013), correlating positively with health outcomes (Hu et al., 2014), a better understanding of the neural underpinnings of impaired emotion regulation in clinical populations would be of immense interest for both the development and the evaluation of new therapeutic interventions. Describing evidence-derived disorder-specific mechanisms for the observed deficits in emotion regulation in clinical populations may thus provide novel targets for pharmacological/cognitive-behavioral interventions or neuromodulation approaches using external [e.g., deep brain stimulation (DBS) and transcranial magnetic stimulation (TMS)] or internal stimulation (e.g., neurofeedback guided emotion regulation). Moreover, identifying a basic mechanism of emotion regulation and demonstrating core deficits spanning different clinical populations may inform research within the Research Domain Criteria (RDoC) framework.

Cognitive regulation of emotion

Due to its efficacy in reducing emotional reactivity, cognitive reappraisal is the emotion regulation strategy most often studied in both healthy and clinical populations. It "changes the way a situation is construed so as to decrease its emotional impact" (Gross, 2002). Use of cognitive reappraisal affects the early stages of the emotion-generative process and therefore decreases both the experience and the behavioral expression of emotion, while other strategies acting later in the emotion-generative process, such as suppression, affect only behavioral expression without changing the experience of emotion (Goldin et al., 2008; Gross, 2002). Cognitive reappraisal entails both self- and situation-focused techniques. Self-focused reappraisal has also been labelled "distancing", as participants are asked to change the emotional impact of a situation by altering its personal relevance, taking the perspective of a detached and objective observer instead of feeling involved. For example, participants are asked to "imagine you were a professional arriving at the scene" or to "imagine your loved ones were involved" to REDUCE or to INCREASE the emotional reactivity to the stimulus, respectively. Situation-focused reappraisal has also been called "reinterpretation", as it aims at re-evaluating the situation by changing its outcomes (e.g., REDUCE: "imagine the situation to be better than initially perceived", INCREASE: "imagine the situation to be worse than initially perceived").

Brain systems involved in emotion regulation

The brain systems supporting cognitive reappraisal of emotion have been investigated extensively in the healthy population. A recent meta-analysis of 23 functional magnetic resonance imaging (fMRI) studies assessing co-activation patterns during reappraisal-mediated downregulation of emotion in healthy participants reported activations in the bilateral dorsolateral prefrontal cortex (dlPFC), ventrolateral prefrontal cortex (vlPFC), dorsal anterior cingulate cortex (dACC), premotor cortex/supplementary motor area (SMA) and inferior/superior parietal cortex (Kohn et al., 2014). A second recent meta-analysis, reviewing 44 fMRI studies on downregulation as well as 12 studies on upregulation of emotion, detected the same regulatory network during downregulation, and a less extended network including only the dACC, left dlPFC and premotor cortex during upregulation (Frank et al., 2014). Systematic modulatory effects were demonstrated in the amygdala/parahippocampal gyrus, which showed decreased activation during down- and increased activation levels during upregulation of emotion (Frank et al., 2014). Finally, results from a third recent meta-analysis, including 48 fMRI studies, converged with previous results showing extensive recruitment of a large regulatory network including the bilateral dlPFC, vlPFC, dACC, premotor cortex/SMA and inferior/superior parietal cortex during both down- and upregulation of emotion and a systematic modulatory influence on the extended amygdala (Buhle et al., 2014). Based on these findings, Buhle and colleagues proposed a key role for both the dlPFC and vlPFC, suggesting that the dlPFC supports the manipulation of appraisals in working memory, while the vlPFC supports the selection and inhibition of appraisals.

In summary, all three meta-analyses converged on describing the same regulatory network, which largely overlaps with the classic frontoparietal cognitive control network. This network includes lateral prefrontal regions (vlPFC, dlPFC) generally implicated in emotion regulation (Ochsner and Gross, 2005; Phillips et al., 2003), but extends beyond this core network to the dACC and inferior/superior parietal cortex, known to be involved in allocating resources during processes that require goal-oriented attention (Cole and Schneider, 2007; Lueckmann et al., 2014). These meta-analyses are in agreement with recent conceptualizations of emotion regulation as supported by a frontoparietal network, with the involvement of the dACC in allocating control (Shenhav et al., 2013) and the inferior/superior parietal cortex in supporting salience detection and allocating attention (Corbetta and Shulman, 2002). The target, the emotional network being modulated, is centered around the amygdala, a region that has been highlighted for its role in processing negative emotion (Costafreda et al., 2008).

These findings can further be extended to studies using electroencephalography (EEG), which allow high temporal resolution (msec) in tracking of emotional arousal. Specifically, an event-related potential, the late positive potential (LPP), is a composite measure indicating the emotional intensity and motivational salience of a stimulus (Hajcak et al., 2010). Indeed, the emotional modulation of the LPP has recently been reported to reflect recruitment of attentional networks during processing of motivationally salient stimuli (Moratti et al., 2011). While the LPP is increased during sustained attention towards salient stimuli, up- and downregulation via cognitive reappraisal increases and decreases the LPP amplitudes, respectively (Hajcak et al., 2010; Hajcak and Nieuwenhuis, 2006; Parvaz et al., 2015, 2012).

Cognitive reappraisal in clinical populations

The goal of the current systematic review is to summarize the literature on cognitive reappraisal of emotion in select neuropsychiatric disorders and discuss the brain networks that are impaired during cognitive regulation of emotion in these clinical populations. Comparison of findings across disorders is aimed to highlight disorder-specific as well as core deficits as potential targets for interventions.

Methods

Study selection

We performed a two-stage systematic literature search to identify fMRI studies investigating cognitive reappraisal in clinical populations. First, we searched Medline/Pubmed using a search term comprised of the method ("fMRI" OR "magnetic resonance imaging" OR "PET" OR "positron emission tomography" OR "EEG" OR "electroencephalography" OR "LPP" OR "late positive potential"), combined with a term related to the disorder ("depression" OR "anxiety" OR "addiction" OR "dependence" OR "schizophrenia" OR "disorder" OR "patient"), and a term referring to the paradigm ("reappraisal" OR "emotion regulation"). Once data extraction was complete, we performed a second manual search for relevant papers based on the reference lists of all included papers. Studies adhering to the following criteria were included:

- Studies published in English, in a peer-reviewed journal, in any year.
- Studies that scanned participants during cognitive reappraisal versus a control condition.
- Studies comparing adults with a DSM-III/IIIR/IV/V diagnosis to a matched control group.
- Studies that reported whole brain results for the group difference.