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http://dx.doi.org/10.1152/jn.00397.2017

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NeuroForum review of Doré, Weber, and Ochsner (2017) published March 8th 2017

Doré, B. P., Weber, L., and Ochsner, K. N. (2017). Neural predictors of decisions to cognitively control emotion. *The Journal of Neuroscience*, 37(10), 2580-2588.

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The author declares no competing financial interests

Acknowledgements

I thank Dr Catherine Thompson and Dr Lynne Marrow for support and insightful discussion.

Key words: emotion regulation, psychopathology, prefrontal cortex, amygdala

Word count: 2,280

Running header: Neural predictors of emotion regulation

Abstract

Emotion regulation is crucial in maintaining healthy psychological wellbeing, and its dysregulation is often linked to a range of neuropsychiatric disorders including depression. The neurobiological underpinnings of cognitive reappraisal, an emotion regulation strategy, have been shown to include the amygdala and regions of the prefrontal cortex. A novel study by Doré, Weber, and Ochsner (2017) has demonstrated that neural activity in these regions during uninstructed visualization of affective stimuli can successfully predict which individuals are more likely to subsequently employ emotion regulation, and under what circumstances.

The ability to respond daily to life's events is crucial to psychological wellbeing, resilience, and physical health. Consequently, emotion regulation, broadly defined as the initiation of a conscious or non-conscious effort to start, stop, or modulate an emotion, has a crucial role in protecting an individual from a range of psychopathologies including anxiety, depression, eating disorders and substance-related disorders (Aldao, Nolen-Hoeksema, & Schweizer, 2010). Therefore, understanding the neurobiological mechanisms supporting emotion regulation will help to develop interventions to improve emotion dysregulation in individuals with a range of disorders.

One such emotion regulation strategy is cognitive reappraisal, where individuals attempt to explicitly reinterpret the meaning of an emotional stimulus or event with the goal of altering the nature, magnitude, or duration of the emotional response (Ochsner, Silvers, & Buhle, 2012). The neuroscientific study of cognitive reappraisal has made significant progress in identifying the neural circuits involved in emotion regulation during the last decade (Buhle et al., 2014; Ochsner et al., 2012). Neuroimaging studies have revealed that emotion regulation recruits a network of regions involved in top-down cognitive control. These include areas of the prefrontal cortex (PFC) including the dorsolateral prefrontal cortex (dlPFC), dorsomedial prefrontal cortex (dmPFC), ventromedial prefrontal cortex (vmPFC) and ventrolateral prefrontal cortex (vlPFC), which allow individuals to apply top-down cognitive control mechanisms. These PFC regions have been shown to regulate (both

up- and down-regulate) activity in the amygdala, a subcortical limbic system structure involved in detecting emotional reactivity via direct and indirect structural connections (Buhle et al., 2014).

Research has recently begun to focus on individual differences in emotion regulation rather than group averages. Within the field of emotion regulation individual variation is not considered statistical noise. Instead, individual differences in the ability to regulate emotion may determine vulnerability and resilience in the face of affective stressors. Consequently, understanding the neural mechanisms underpinning individual differences in successful emotion regulation may aid clinical assessment of interventions and provide more effective translational therapies.

Facial electromyography, a technique that measures muscle activity by recording electrical impulses when muscle fibres contract, can be employed to index an objective measure of trait-like individual differences in emotion regulation and is able to predict amygdala-PFC functional connectivity (Lee, Heller, van Reekum, Nelson, & Davidson, 2012). Moreover, using diffusion tensor imaging, it has been shown that increased use of emotion regulation is predictive of stronger amygdala-PFC microstructure fibre tract pathways, whilst trait anxiety is negatively correlated with amygdala-PFC connectivity (Eden et al., 2015). These studies adopting individual difference approaches demonstrate that PFC regions and the amygdala are implicated in emotion regulation at both the anatomical and functional level in healthy individuals.

Whilst progress has been made towards identifying brain circuits involved during emotion regulation, it remains unknown whether neural mechanisms can be used to predict emotion regulation decisions. Previous research investigating the neural circuitry underpinning emotion regulation has not given participants the choice as to whether or not to regulate their emotion, and instead employed experimental designs where individuals are instructed to adopt emotion regulation strategies and neural activation is recorded. Consequently, the neural mechanisms predicting the decision to regulate emotional responses were until recently unknown. This has important implications as the decision to purposefully regulate one's negative emotion has been shown to be a protective factor for well-being (Sheppes et al., 2014). A recent study by Doré et al. (2017) has provided some novel insights to this

issue. Here the authors attempted to a) reveal the neural processes supporting individual decisions to regulate emotional responses, and b) determine whether brain activity can be used to predict emotion regulation decisions.

Participants initially underwent training in the emotion regulation strategy cognitive reappraisal to ensure they understood what a choice to regulate emotion would involve. This included experimenter-guided training in positive reappraisal (i.e. focussing on the potential positive aspects of a negative stimulus or situation) and minimizing reappraisal (i.e. focussing on potential neutral aspects of a negative stimulus or situation). Participants then completed an emotion regulation task where they were able to practice using these strategies. Subsequently, the researchers determined brain regions known to be involved in emotion regulation on an a priori basis (vlPFC, dlPFC, dmPFC, and amygdala), and used functional magnetic resonance imaging (fMRI) to record activity from these areas during a negative image viewing task. Participants were required to view a series of negative images and rate how positive and how negative the images made them feel using a 5-point scale ('How positive do you feel' and 'How negative do you feel'). Importantly, participants were free to think about the images in any manner and were not instructed to regulate their emotional response to the images. The second part of the study, completed outside the fMRI scanner, involved an emotion regulation choice task in which participants were presented with negative images (some previously seen in the initial image viewing task and some novel images) and asked to decide whether to regulate their emotion or simply to view the images passively. Participants recorded their emotion regulation decision by selecting either 'look naturally' or 'reappraise' in response to each image.

This paradigm allowed Doré and colleagues to demonstrate that specific neural mechanisms, engaged during uninstructed visualization of emotional stimuli, are able to successfully predict subsequent behavioural choices concerned with the regulation of emotional response. At the individual level, using a model-based analysis, more frequent decisions to employ cognitive reappraisal were predicted by greater activity in the vlPFC, dlPFC, dmPFC, and amygdala. These results were similar for both old and new images in the emotion regulation choice task. Further, these relationships were still evident after controlling for self-report ratings of positive and negative affect,

demonstrating that increased activation of these neural circuits during the viewing of negative images predicted the decision to regulate emotion independently of participant's subjective emotional experience whilst viewing negative images. Moreover, Doré and colleagues also investigated whether brain activity could predict the specific events for which the decision to regulate emotion is most likely. This was operationalized by conducting analysis at the level of the stimulus and by using a whole brain activity pattern that had previously been shown to be associated with emotion reappraisal (Buhle et al., 2014). At the stimulus level, trial-to-trial differences in whole brain pattern activity predicted the decision to regulate emotion to a specific stimulus. A model including this distributed brain pattern, in addition to PFC and amygdala regions, performed better at predicting the decision to regulate emotion to a given stimulus than a model only including self-report data and affective ratings of stimuli. This result demonstrates that stimulus-level variability in brain pattern expression can be used to predict which stimuli individuals are more likely to employ cognitive reappraisal.

Doré et al. (2017) revealed important findings moving towards a more individualized science of emotion regulation (Doré, Silvers, & Ochsner, 2016) and translational neuroscience approach – going beyond experimentally directed emotion regulation and instead being able to predict who will freely choose to regulate their emotion and under what circumstances. Using individual variability in neural responses to negative stimuli, it was demonstrated that decisions to deploy cognitive control of emotion can be predicted by neural processes during earlier emotional experience. However, due to the nature of the correlational design, it is not possible to make any inferences about causality in the relationship between neural activation during affective experience and subsequent decisions to regulate emotion. Future experimental work should build upon these findings using neurostimulation techniques such as repetitive transcranial magnetic stimulation (rTMS) and/or transcranial direct current stimulation, which allow for experimental manipulation of specific neural circuits. For instance, rTMS has recently been used to causally infer that inhibitory disruption of the right dlPFC influences early affective processing as evidenced by altered neurophysiological response and impaired behavioural performance (Zwanzger et al., 2014).

The investigation of negative emotion regulation and/or dysregulation is of central importance to understanding the neural mechanisms involved during emotion regulation in healthy individuals and clinical populations. However, within the emotion science literature it has been documented that a bias exists whereby positive conditions (e.g. positive mood, positive experimental stimuli, or positive emotion regulation conditions) are often not included, and this limits the conclusions that can be made about affective processing. There are instances when individuals need to regulate positive emotional experiences, and currently the neural processes involved during such responses are less well understood. Thus, it is recommended that future research includes both positive and negative experimental conditions.

In Major Depressive Disorder increases in dlPFC activity when regulating emotion has been shown to predict reductions in symptom severity in depressive patients (Heller et al., 2013). However, it is unknown whether the neural circuits underpinning the decisions to regulate emotion are able to predict behaviour and symptom severity reduction in clinical populations. Doré et al. (2017) indeed suggest that future work could investigate whether clinical disorders show disruption in their ability to deploy emotion regulation, and importantly research needs to focus on instances of uninstructed emotion regulation (i.e. investigations of the decision whether to regulate emotion rather than experimental designs where individuals are explicitly told to regulate their emotion). Crucially, however, research adopting a more individualized approach to the investigation of the decision to regulate emotion needs to move beyond the laboratory adopting study designs better able to capture real-world behaviour. Using fMRI it has been demonstrated that dlPFC activity in response to reward responses recorded in the laboratory are able to predict behavioural reactivity of real-world positive emotion. This relationship was established by correlating dlPFC activity with behavioural response following a reward given in natural environments (Heller et al., 2015). Future translational neuroimaging investigations of emotion regulation decisions should aim to adopt such techniques. Consequently this will help to understand the neural basis of such decision making in healthy individuals and patient populations in real-world settings, and aid in the development and evaluation of therapeutic interventions.

Although not discussed in detail by Doré et al. (2017), their finding also showed that bilateral precuneus activity were positively correlated with emotion regulation decisions. The precuneus, part of the posteromedial portion of the parietal lobe, has been shown to be involved in broad aspects of cognition including production/alteration of subjective experience, integration of internal and external information, visual mental imagery, episodic memory recall, and self-referential processing (for a review see Cavanna & Trimble, 2006). Further, recent evidence has suggested that this cortical area forms part of the neural circuit activated during another emotion regulation strategy – attentional deployment – where attention is directed with the goal of changing one's emotional response (Ferri, Schmidt, Hajcak, & Canli, 2016). Ferri and colleagues demonstrated that task-dependent coupling between the precuneus and amygdala is increased during visual attentional deployment, suggesting that the precuneus is involved in the regulation of amygdala reactivity to emotional stimuli when emotion regulation involves shifts in attention. Moreover, the strength of coupling between the precuneus and amygdala predicted attentional deployment success, and individual differences in trait reappraisal were positively correlated with amygdala-precuneus connectivity. Considering these observations in combination with those of Doré et al. (2017) suggests that the precuneus may be part of a network of neural circuits involved in multiple emotional regulation strategies. Indeed, it has been suggested that individuals may simultaneously use attentional deployment and cognitive reappraisal during emotion regulation (see Ferri et al., 2016). However, as the precuneus was not identified as a brain region of interest on an a priori basis by Doré and colleagues (in relation to its involvement in cognitive reappraisal), caution is needed when interpreting this observation. Further research is needed to reveal the precise role of the precuneus in emotion regulation (see below).

Doré et al. (2017) have provided evidence to suggest that neural activity during affective experience can predict the individuals who are more likely to subsequently deploy cognitive control of emotion, and for what stimuli emotion regulation is most likely. This novel methodology should help to direct emotion regulation research towards a more individualized translational neuroscience approach. A number of avenues for future research have been identified. Firstly, researchers need to include positive emotion conditions within their experimental designs to test whether the neural

mechanisms evident during negative emotion regulation are similar to those adopted during positive emotion regulation. Additionally, the use of neurostimulation techniques will allow researchers to infer causality between underlying neurobiological mechanisms and emotion regulation. It will also be advantageous for research to adopt study designs that allow the measurement of real-world behaviour in both healthy individuals and clinical populations. This will be crucial for the development and evaluation of translational therapeutic interventions. Further, an individualized approach that acknowledges the role of the individual in emotion regulation will aid development of our understanding of individual difference traits that can be targeted for therapeutic intervention. Lastly, recent evidence has suggested that the precuneus may be part of the neural circuit involved in emotion regulation, and future work should try to reveal the exact role of this brain region. For example, it is not known whether the primary involvement of the precuneus during emotion regulation is related to the alteration of subjective experience, integration of internal and external information, self-referential processing, attentional deployment, or a combination of these processes.

In summary, using an elegantly designed study adopting an individualized translational neuroscience approach, Doré et al. (2017) revealed that increased neural activation in the PFC and amygdala during uninstructed affective experience can successfully predict individuals who are more likely to regulate their emotional responses. Further, trial-to-trial variability of a brain activity pattern previously shown to be related to emotion regulation was able to predict emotion regulation at the stimulus level. This novel approach to the study of emotion regulation will be especially valuable when applied to clinical populations and the development of translational therapeutic interventions.

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