

1 **The neural mechanisms able to predict future emotion regulation decisions**

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20 **Abstract**

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

28

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

36 One such emotion regulation strategy is cognitive reappraisal, where individuals attempt to
37 explicitly reinterpret the meaning of an emotional stimulus or event with the goal of altering the
38 nature, magnitude, or duration of the emotional response (Ochsner, Silvers, & Buhle, 2012). The
39 neuroscientific study of cognitive reappraisal has made significant progress in identifying the neural
40 circuits involved in emotion regulation during the last decade (Buhle et al., 2014; Ochsner et al.,
41 2012). Neuroimaging studies have revealed that emotion regulation recruits a network of regions
42 involved in top-down cognitive control. These include areas of the prefrontal cortex (PFC) including
43 the dorsolateral prefrontal cortex (dlPFC), dorsomedial prefrontal cortex (dmPFC), ventromedial
44 prefrontal cortex (vmPFC) and ventrolateral prefrontal cortex (vlPFC), which allow individuals to
45 apply top-down cognitive control mechanisms. These PFC regions have been shown to regulate (both

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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