Commentary

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Decoding Emotion: The Amygdala–Prefrontal Cortex Pathway for Emotion Regulation of Children

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Emotion regulation is generally conceptualized as involving the awareness of emotions and the flexible modulation of emotional responses to meet individual goals and situational demands. Theoretical analysis has postulated a multilayered process where a low-level process generating emotion and the consequent responses is iteratively evaluated and modulated by a higher-level regulatory process (1). Despite its potential link to clinical conditions such as anxiety and depressive symptoms, it remains largely unknown how emotion regulation is implemented in the distributed neural network in the brain.

In the current issue of *Biological Psychiatry*, Warren *et al.* (2) addressed this question by taking a novel computational approach to model emotion regulation as parametric modulation of an integration-to-bound process and by linking it to the interaction between the amygdala and the dorsolateral prefrontal cortex (DLPFC). In their reappraisal task, 45 children 10 to 11 years of age were guided by an instructional cue to positively re-evaluate aversive images. After viewing the images, the children rated the extent of adverse emotion they had experienced, which was compared with the ratings made after viewing similarly aversive images without the reappraisal. Reappraisal is regarded as a regulatory tactic to alleviate negative emotion originally formed in response to a triggering experience by altering the way the experience is interpreted, and the current state is adversely represented (1). The children rated aversive stimuli as less unpleasant during the reappraisal condition compared with the aversive condition without the reappraisal.

In their novel and intriguing approach, Warren *et al.* (2) modeled emotion perception as a drift-diffusion process, suggesting that reappraisal might regulate emotion perception by altering the parameters of the drift-diffusion process. Sequential sampling models, of which the drift-diffusion model (DDM) is a special instance, are often interchangeably referred to as integration-to-bound models and have been extensively applied to analyze simple 2-choice decisions in the domain of perceptual decision making (3). The general idea of such models is that noisy, momentary evidence supporting one hypothesis over the other alternative hypothesis is integrated over time ("sequential sampling of evidence") and that a decision is made when the accumulated evidence reaches one of the two decision thresholds or boundaries ("integration-to-bound") (Figure 1). Evidence is typically represented as a normally distributed random variable with its mean and variance reflecting the strength of evidence and random noise, respectively. Choice and response time are largely determined by two key parameters of the model: drift rate, which captures the relative strength of evidence over noise, and threshold, which sets the number of samples needed before committing to a decision given the evidence.

Warren *et al.* (2) recoded emotion rating as a categorically non-negative or negative state and mapped the two states to positive and negative thresholds, respectively (Figure 1). They then estimated the parameters of the DDM separately for the aversive and the reappraisal conditions. Several findings are notable. First, the drift rate was estimated to be higher across the participants during the reappraisal condition than the aversive condition. Within the framework of DDM, the drift rate shifted toward positive value, suggesting that the input evidence entering the integration process was more positively evaluated during the reappraisal condition compared with the aversive condition. Second, the initial position of the accumulated evidence at the beginning of the evidence integration was estimated to be slightly biased toward the threshold for positive emotion. Although the contribution of this adjustment to the success of the reappraisal seems to be minimal, positive initial bias prior to the integration process effectively lowers (heightens) the threshold for positive (negative) emotion, favoring a decision toward positive emotion, in the sense that given the evidence, the accumulated evidence is more likely to reach the positive threshold because it requires fewer samples than reaching the negative threshold. Finally, trait anxiety and stress reactivity measured with Behavioral Assessment System for Children and the Response to Stress Questionnaire, respectively, were negatively correlated with such parameters of the DDM during the reappraisal, suggesting a potential link between reappraisal via the drift-diffusion process and the general level of anxiety and response to stress.

Warren *et al.*'s proposal (2) parallels a recent conceptual development that analyzes emotion perception and recognition as active inference, in which a hidden emotional state is inferred based on interoceptive evidence and external contexts, in combination with a generative model of emotion (4). The dynamic integration-to-bound model can be conceived as a proposal for a possible algorithmic and implementational mechanism of the inference. Although sequential sampling models, including DDM, have been mainly applied to the domain of perceptual decision making, recent studies show that they can be extended to account for a broader range of phenomena in nonsensory and cognitive domains, such as economic decision making, foraging, and reasoning (5–7). This trend suggests a possibility that the integration-to-bound

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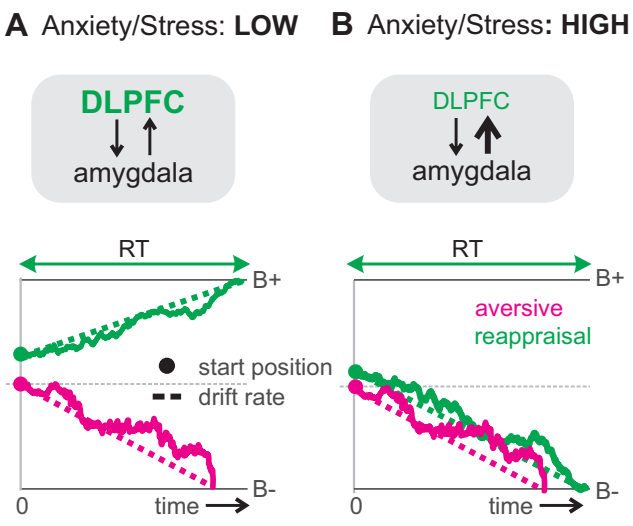

Figure 1. Emotion regulation and the amygdala–dorsolateral prefrontal cortex (DLPFC) pathway. Schematics of the right amygdala–DLPFC pathway (top) and the drift-diffusion process (bottom) that are differently modulated during reappraisal in the children with **(A)** low or **(B)** high levels of trait anxiety and stress reactivity. (Top panels) Arrows indicate the direction of causal influence, with a thicker arrow indicating the strengthened influence during the reappraisal. (Bottom panels) Examples of time-varying trajectory of the accumulated evidence are shown for the aversive (red) and the appraisal (green) conditions. B+, decision boundary for positive (non-negative) emotion; B−, decision boundary for negative emotion; RT, response time.

process might reflect a canonical neuroanatomical circuit distributed in the brain that mediates evidence-based inference across domains, including emotion.

Despite the general success in explaining basic behavioral data, it has been challenging to identify the neural correlates of the presumed integration-to-bound process in the brain. For instance, the trajectory of the accumulated evidence gradually ramping up (down) over time is the signature of DDM, which was widely used to fit the behavioral and neural data. However, neural signals exhibiting similar dynamics can be also observed across multiple contexts (e.g., increasing urgency) that do not necessarily involve an integration process, suggesting that the ramping activity alone might not be sufficient to test and probe the presumed evidence integration in the brain (8). It was also shown that the ramping trajectory can emerge from averaging neural activity over multiple trials, even when the activity undergoes a discrete step-like change at the level of a single trial (9). Warren *et al.* (2) reported that the neural activation in the DLPFC inferred from the blood oxygenation level–dependent signals was correlated with the drift rate estimated with the simple DDM. However, given the aforementioned challenges, Warren *et al.*'s results (2) have not yet provided compelling and conclusive evidence for the hypothesized integration-to-bound process, as the DLPFC activation correlated with the drift rate alone cannot provide sufficient evidence either for or against the process in the brain. The temporal dynamics in the blood oxygenation level–dependent signals need to be rigorously analyzed. Moreover, response time distributions often provide rich data that are sensitive to the changes in the parameters and the form of the integration-to-bound process, and it is useful to carefully analyze the characteristics of response time distribution beyond mean response time. Another useful strategy would be to use a dynamically changing stimulus that predicts more complex dynamics than the simple, ramping trajectory in the accumulated evidence, which can provide the resolution required to test the integration process against other competing hypotheses (10). In addition, generalized and extended models would allow more granular analysis of various features, such as timescale of integration (e.g., leaky vs. perfect integration), independent and/or interacting integrators (e.g., lateral inhibition), and time-varying boundary, etc. (3). In these regards, Warren *et al.*'s results (2) raise further questions such as whether and how the effect of anxiety and stress can be modeled within the integration-to-bound framework if the levels of anxiety and stress are directly manipulated during the reappraisal. Conversely, other open questions would be whether the perception of anxiety can be also modeled as an integration-to-bound process and whether/how anxiety perception might be influenced by the outcome of emotion regulation.

Warren *et al.* (2) analyzed the blood oxygenation level–dependent signals using functional magnetic resonance imaging and noted that the causal influence directed from the right amygdala to the right DLPFC tended to become stronger during the reappraisal for the children with a higher level of anxiety and stress reactivity. Moreover, the right DLPFC tended to be more active in those children for whom the drift rate changed more positively during the reappraisal compared with the aversive condition (Figure 1), suggesting that the heightened level of anxiety and stress might disrupt the reappraisal via the strengthened influence from the amygdala to the DLPFC. While these results might provide potentially important insights into the circuits that underlie the etiological link between emotion regulation and anxiety, inference about directed influence needs to be made with caution when it is based on correlations and requires taking into account comprehensive correlational structures among all the relevant variables to avoid spurious correlations. For example, an alternative interpretation of the results can be that the correlated changes in the DLPFC activation, the drift-diffusion process, and amygdala–DLPFC connectivity might reflect a circuit responding to the anxiety and stress that can be differentially experienced as the consequence of the successful or failed reappraisal.

Warren *et al.*'s study (2) shows the potential of this computational approach, bringing a new perspective to the research on emotion regulation, but many open questions remain, such as what might be the signals that constitute the evidence for emotion perception, whether the integration-to-bound process takes place in the DLPFC or other regions, how the activation of DLPFC modulates specific parameters of the process (e.g., drift rate), and whether the amygdala is involved in the integration-to-bound process in more specific ways than simply modulating the level of activation in the DLPFC.

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Article Information

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