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To Apply Yourself Is Human, to Reapply Divine

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Prefrontal cortex is involved in adapting our emotional response to setbacks. While we feel that some setbacks are controllable, others are not. Here, Bhanji and Delgado (2014) reveal the neural substrates of persistence in the face of controllable and uncontrollable setbacks.

Would you reapply for a job with a company that previously rejected you? Think about it. Imagine there were two professors currently employed at Dartmouth College. One applied, and he was hired on his very first try (we'll call him Bill in this example). Imagine that the other; well, he needed more chances before his eventual hire (we'll call him P.W. to protect his identity). What dictates whether someone will persist when they encounter a setback? Is it the person who remains calm in the moment, not letting this single event rattle her? Or is it the person who reacts strongly to defeat and heavily reinvests in the project, determined to change things the next time? To borrow from Shakespeare, tell us where is persistence bred, or in the heart, or in the head (*The Merchant of Venice*, 3.2)? In this issue of *Neuron*, Bhanji and Delgado (2014) provide clear evidence of the latter.

Bhanji and Delgado (2014) used fMRI of subjects from a college community as they made choices about academic degree paths. The study was designed to hand the "students" setbacks along the way and then gauge whether the brain's response to the setbacks could predict how persistent an individual would be on subsequent choices. Specifically, students first selected one of three "academic degree" paths that could earn them a low, medium, or high payoff. As students progressed down their degree path, they encountered obstacles in the form of "exams" and "class cancellations." For exam trials, students had to guess the correct answer (i.e., correctly select one of four buttons to pass the exam) and were then told whether they passed or failed the exam. For class cancellation trials, students signed up for a class by selecting one of four buttons, and then the computer randomly canceled one of the classes. If the student failed an exam or their class was canceled, they had to start over. The authors also measured how disappointed students felt following setbacks.

Critically, after having to start over, the student had to choose whether they would try to redo the same degree path (i.e., persist) or select a new one. Bhanji and Delgado (2014)'s clever twist was that in the "take an exam" scenario, students were led to believe that there was a correct answer. Failing the exam, then, was a controllable setback; much like a real student on an academic degree path, they could do better the next time. By contrast, students believed that having a class canceled in the "sign up for a class" scenario was a setback that was out of their control—students selected a course, and then one course was randomly chosen by computer to be canceled. Behavioral research (Andrews and Debus, 1978) has shown that we are more likely to persist when we believe we have control over a situation. Of interest to Bhanji and Delgado (2014) was whether the neural underpinnings of persistence to a controllable setback would differ from those of uncontrollable setbacks in the face of an ensuing negative affect change.

Consistent with prior work (Andrews and Debus, 1978), Bhanji and Delgado (2014) found that subjects were more likely to persist after controllable setbacks (failing an exam) compared to uncontrollable setbacks (having a class canceled by the computer). Interestingly, the disappointment (i.e., negative affect) associated with the setbacks did not differ between controllable and uncontrollable ones. Surprisingly, however, the students that showed the greatest negative affect after a setback were more likely to persist, regardless of whether the setback was uncontrollable or controllable. Thus, it would appear that higher motivational investment in the task at hand and subsequent feedback predicts good outcomes in terms of persistence.

In terms of brain activity, the study shows that activity within two different brain regions predicts whether subjects persist, depending on whether the setback was controllable or uncontrollable. For uncontrollable setbacks (i.e., cancelled class), signal changes within the ventromedial prefrontal cortex (vmPFC) predicted how likely subjects were to persist down the same path. Further analysis revealed that this vmPFC activity mediated the relationship between negative affect and persistence. By contrast, a brain region commonly associated with reward value, the ventral striatum, predicted persistence following controllable setbacks.

The vmPFC is necessary for regulating our emotional responses. Our ability to recruit this brain region predicts the extent to which we are able to interpret emotional experiences in a positive light. This is true whether this event is the surprised face of another person (Kim et al., 2003), a personality attribute that may or may not describe us in a positive or negative light (e.g., confident) (Moran et al., 2006), a photograph of something unpleasant (e.g., car crash victims) (Ochsner and Gross, 2005), or a simple tone that once predicted a shock but now no longer does (i.e., extinction) (Phelps et al., 2004; Milad and Quirk, 2002). In these examples, vmPFC activity may diminish the effects of negative affect, downregulate it, and permit the more flexible behavior. What is new here is that Bhanji and Delgado (2014) interpret their mediation data to suggest that when

negative affect accompanies uncontrollable setbacks, as is often the case, the vmPFC activity is necessary to adapt to the emotional reaction and, in so doing, preserve persistence. It's an intriguing idea, suggesting that the vmPFC might regulate adaptive outcomes in different ways depending on the outcome goal. Sometimes suppressing an emotional response is the goal, like when we had to calm ourselves before taking our driver's license road test when we were 16. But perhaps when we perceive a stressor to be uncontrollable, as in the present study, the negative affect change is the catalyst that kicks vmPFC into a higher gear and effects adaptive change (i.e., persistence). Downregulating this emotional response may not be the goal in this case.

The ventral striatum on the other hand is important for signaling prediction errors when behavioral outcomes do not match our expectations (Li et al., 2011; Schönberg et al., 2007; Sutton and Barto, 1998). "Failing the exam" is a controllable setback in the Bhanji and Delgado (2014) paradigm because students are given the opportunity to either retake the exam or choose a new degree path. There is value in "staying the course," as the authors note, because the students can eliminate an incorrect exam response. This is not the case for "class cancellations," as the computer will just randomly cancel a different class every time. The important distinction here, then, is that when we believe we have control over situations, the ventral striatum can use value signals to motivate future behavior. Bhanji and Delgado (2014) cite previous work (LeDoux and Gorman, 2001; Gross, 1998; Folkman and Lazarus, 1988) to support this notion and very interestingly contrast this striatal effect as problem focused compared to the prefrontal effect that is more emotion focused.

Bhanji and Delgado (2014)'s data offer an intriguing model that suggests two distinct neural routes that can result in more persistent behavior in the face of a setback: a ventral striatum route that is focused on value that may encourage persistence in instances where the setback is self-inflicted and can be corrected, and a vmPFC route that can adapt to the kinds of negative emotions that often accompany setbacks that are out of our control and might otherwise encourage us to give up or change course. As with all novel findings, this work offers many intriguing possibilities for future research into how and when to remain persistent in the face of adversity and the neural architecture that subserves such persistence. The ability to delineate controllable from uncontrollable setbacks comes to mind here. Did P.W. suffer a setback in his first Dartmouth interview because of something he did (e.g., humming inappropriately in his meeting with the Dean) or was he doomed to fail because of a cancelled job search? In the former case, his ventral striatum might guide him to reapply sans the humming. In the latter case, it is his ability to recruit his vmPFC to consider his hard feelings toward Dartmouth in a more flexible light that may allow him to try again the next three times. To borrow from Alexander Pope (*Essay on Criticism*, 1711), to apply is human, to reapply divine.

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