Exaggerated control demands over reward-related behavior in anorexia nervosa

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Keywords: task-positive network, reward, reinforcement learning, self-control, eating disorders

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Commentary

Anorexia nervosa (AN) is a debilitating disorder characterized by an almost inconceivable endurance in the face of self-induced starvation and its physiological and psychological sequelae. While the pervasive effects of extensive weight loss on well-being have been detailed vividly since the seminal Minnesota Starvation experiment (1), we are only beginning to unravel the neurobiological mechanisms subserving AN. Intuitively, one might expect that individuals suffering from AN lack this inherently strong drive to actively seek and consume food when they are hungry. This lack of motivation could arise either from a blunted response to reward in general or, more specifically, an attenuation of homeostatic feedback signals modulating reward responsivity in healthy individuals according to the current metabolic state. Despite its intuitive appeal, empirical support for this "reward deficit" theory has been inconclusive to date and there is conflicting evidence suggesting that a generalized blunting of reward responsivity is not a trait marker of AN (2). Instead, it has been recently proposed that other aspects of reward-based learning (3) or, more broadly, cognitive control over actions and their consequences may constitute better trait markers of AN (2, 4). However, dissociating the commonly entangled components of motivated behavior such as valuation, learning, and action control is not a trivial endeavor and requires detailed behavioral and neurobiological mapping of responses. To this end, computational modeling and model-based analyses of neuroimaging data offer promising tools to decompose reward-related behavior.

Consequently, in this issue of *Biological Psychiatry*, Bernardoni et al. (5) investigated AN patients and matched healthy controls performing a reinforcement learning task inside the MR scanner. In the task, participants had to choose one of two options. Selecting the "good" option was associated with a high probability of winning whereas selecting the "bad" option was associated with a high probability of losing money. However, participants not only had to identify the best option at a given moment. Crucially, they also had to keep track of eventual changes in reinforcement because the contingencies of winning or losing would be eventually swapped (or "reversed") if they continued to exploit the best option. Intriguingly, Bernardoni et al. (5) found that AN patients showed increased learning rates after losses, which was echoed in an increased blood-oxygen-level dependent (BOLD) response in the posterior medial frontal cortex (pMFC). Collectively, behavioral and neural results were indicative of a greater sensitivity to losses in AN patients compared to matched healthy controls.

One notable advance for research on eating disorders comes via the combined use of behavioral and neural data within a well-defined computational framework employed in the study. Thereby, Bernardoni et al. (5) identified a basic mechanism in reward-based learning that may contribute to the etiology of AN. Whereas pioneering research in the eating disorder field has previously highlighted alterations in reward-based learning in patients suffering from AN (6) or bulimia nervosa (7), such conditioning tasks cannot be employed for model-based analyses based on estimates derived from individual behavior on the task (8). However, the behavioral facet of reinforcement learning is essential in

providing more refined mechanistic insights into how reward-based learning is implemented in a particular region of the brain as opposed to only identifying where alterations in reward processing occur in the brain (8). Moreover, behavioral observations can provide important constraints on plausible results at the neural level. In combination with mathematical constraints in computational models, we can thereby derive formalized and testable predictions for other related tasks that might ultimately help to elucidate core mechanisms contributing to psychopathology.

Whereas this focus on well-defined neurobiological substrates, driving pathological behavior is pivotal in advancing our understanding of biomarkers for eating disorders ("precision psychiatry"), it is important to factor in model complexity in this cause. Such a penalty for complex explanations is inherent in computational modeling, but needs to be employed at the construct level of reward as well to unravel relevant facets for AN. At first glance, the hypothesized alterations in reward-based learning versus cognitive overcontrol of reward-related behavior might seem as competing explanations, although they can be incorporated in a common framework of reinforcement. For example, recent studies (2, 3, 5) have highlighted alterations in reward processing between AN patients and healthy controls in distinct brain regions (Figure 1). Yet, many of the highlighted brain regions showing group differences across these reward tasks are part of the task-positive network (TPN). Thus, a parsimonious account for these results might be that employing or updating a given action policy could be assigned a higher value (relative to rest or no control) in patients with AN. Such an extension could be easily incorporated within the expected value of control (EVC) framework (9) by assigning individual valuation weights to executing or updating a control demand. Notably, the dorsal anterior cingulate cortex (dACC) and the pMFC play a critical role in computing the EVC, which dovetails well with the results by Bernardoni et al. (5).

Related to the challenge of integrating findings into a coherent framework of reward-related behavior, several key questions concerning specificity remain open for future work along the lines of Bernardoni et al. (5). For example, greater sensitivity to punishment may also be (partly) explained by the greater informational value provided by negative feedback when reinforcement schedules give you an edge in winning by correctly identifying the good option. In other words, once you have figured out what the best option is, punishments occur less frequently until a reversal occurs in the task. Tuning one's sensitivity to punishment may thus be a beneficial strategy in seizing the information provided by the task to readapt behavior accordingly. Thus, facilitated learning in the face of negative outcomes could also be driven by an intrinsic incentive to do maximally well (4). Moreover, it remains to be determined if the increased incentive value of exercise versus rest, which is commonly reported in patients with AN and affected by dopamine tone in healthy individuals (10), might be associated with individualized weights assigned to action control policies, regardless of the instrumental value of behavior. Clearly, such vital questions will need to be addressed in the iterative process of developing and refining generative models of reward-related behavior that can account for characteristic behavioral phenotypes across a more diverse set of reward tasks.

To conclude, the study by Bernardoni et al. (5) provides a major step in advancing precision psychiatry at the methodological and conceptual level within the field of eating disorders. By highlighting a key mechanism for altered reinforcement learning in patients with AN in both behavioral and neural responses, Bernardoni et al. (5) demonstrate how model-based analyses of fMRI data may help to further elucidate the core components within the heterogeneous domain of reward processing underlying psychopathology. Nevertheless, computational approaches to reinforcement will also help in integrating emerging findings across different tasks once they are employed with the same rigorous principles to multiple tasks and diverse patient samples. Hence, there is not only great need for an improved understanding to refine future treatment. There is also well-grounded hope that this novel set of tools may yield essential insights into the etiology of AN and other disorders affected by altered control over motivated behavior.

Acknowledgement

The work was supported by the fortune grant #2453-0-0 provided by the University of Tübingen. I declare that there is no conflict of interest. This commentary benefited from helpful discussions with Caroline Burrasch, Monja P. Neuser, and Vanessa Teckentrup.

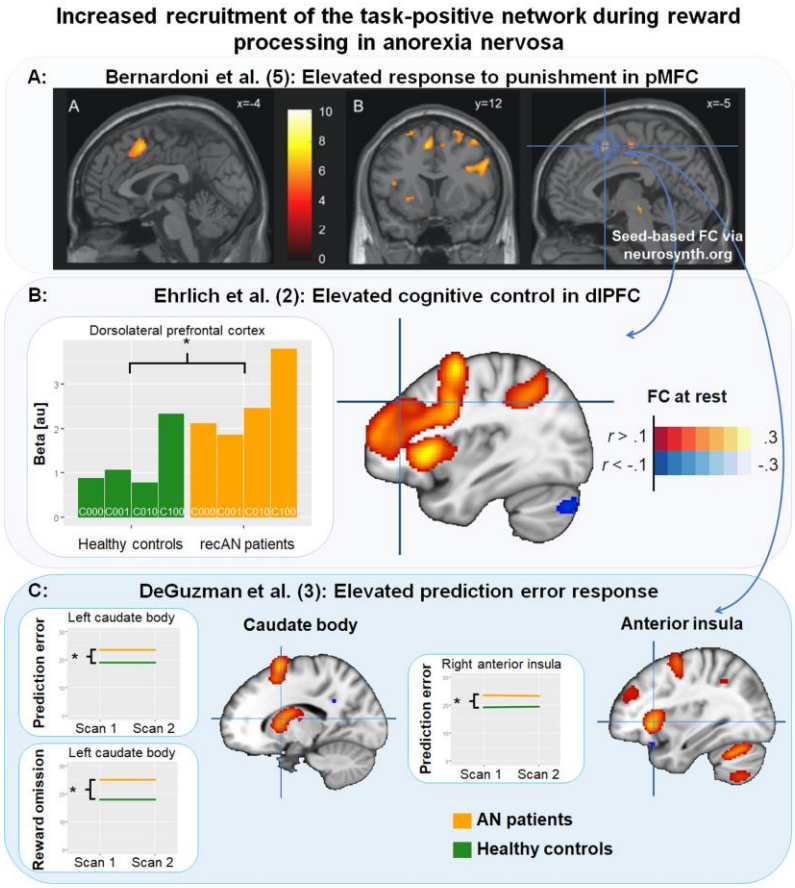

Figure 1: Convergence of recent findings pinpointing alterations in reward processing onto the task-positive network (TPN) across tasks and studies. A: Based on the peak difference between patients with anorexia nervosa (AN) versus healthy controls from Bernardoni et al. (2018), a seed-based functional connectivity (FC) analysis using neurosynth.org indicated that recently observed differences recruit a similar co-activation network, resembling the TPN (meta-analytic co-activation terms "task" r = .59, "tasks" r = .50, "working memory" r = .47). In Ehrlich et al. (2015), recovered AN (recAN) patients showed elevated activation, regardless of magnitude, to monetary cues signaling the incentive for impending effort in the dlPFC as well as altered feedback processing after receiving the outcome, suggestive of elevated cognitive control (b). In DeGuzman et al. (2017), acute AN patients showed elevated prediction error responses during a monetary reward tasks within the reward circuit encompassing the TPN. These results also indicate faster updating of learned values which form the basis for action control via the TPN.

References

1. Kalm LM, Semba RD (2005): They starved so that others be better fed: Remembering Ancel Keys and the Minnesota experiment. *J Nutr*. 135:1347-1352.
2. Ehrlich S, Geisler D, Ritschel F, King JA, Seidel M, Boehm I, et al. (2015): Elevated cognitive control over reward processing in recovered female patients with anorexia nervosa. *J Psychiatry Neurosci*. 40:307-315.
3. DeGuzman M, Shott ME, Yang TT, Riederer J, Frank GKW (2017): Association of elevated reward prediction error response with weight gain in adolescent anorexia nervosa. *Am J Psychiatry*. 174:557-565.
4. Wagner A, Aizenstein H, Venkatraman VK, Fudge J, May JC, Mazurkewicz L, et al. (2007): Altered reward processing in women recovered from anorexia nervosa. *Am J Psychiatry*. 164:1842-1849.
5. Bernardoni F, Geisler D, King JA, Javadi A-H, Ritschel F, Murr J, et al. (2018): Altered medial frontal feedback learning signals in anorexia nervosa. *Biol Psychiatry*. 83.
6. Frank GK, Reynolds JR, Shott ME, Jappe L, Yang TT, Tregellas JR, et al. (2012): Anorexia nervosa and obesity are associated with opposite brain reward response. *Neuropsychopharmacology*. 37:2031-2046.
7. Frank GK, Reynolds JR, Shott ME, O'Reilly RC (2011): Altered temporal difference learning in bulimia nervosa. *Biol Psychiatry*. 70:728-735.
8. O'Doherty JP, Hampton A, Kim H (2007): Model-based fMRI and its application to reward learning and decision making. *Ann N Y Acad Sci*. 1104:35-53.
9. Shenhav A, Botvinick MM, Cohen JD (2013): The expected value of control: an integrative theory of anterior cingulate cortex function. *Neuron*. 79:217-240.
10. O'Hara CB, Keyes A, Renwick B, Leyton M, Campbell IC, Schmidt U (2016): The effects of acute dopamine precursor depletion on the reinforcing value of exercise in anorexia nervosa. *PLoS One*. 11:e0145894.