

Brain, Reward, and Eating Disorders: A Matter of Taste?

Humans view food in unique ways, eating to meet not only basic homeostatic needs but also sensory, emotional, and sociocultural ones. For the majority of people, eating is a source of pleasure and gratification. However, individuals suffering from eating disorders such as anorexia nervosa develop a strong motivation to reject food for long periods of time, with dramatic effects on health, relationships, and productivity. Despite the relevance of eating disorders in our society and substantial research efforts over the past decade, information on the underlying mechanisms remains incomplete, even at a basic level.

The accumulated knowledge to date points to a broad neurodevelopmental framework for the etiology of anorexia nervosa (1). According to this model, the illness results from the interaction between predisposing factors and compensatory responses to chronic stress once a certain threshold is crossed and an out-of-control vicious circle is established. Dysregulation of reward processing mechanisms is believed to play a central role downstream in this complex scenario, contributing to the development and maintenance of core symptoms (2, 3). Recent conceptualizations of reward in anorexia nervosa suggest that the specific dysfunction consists of a suppression of the desire to eat (“wanting”) while the capacity to hedonically evaluate food (“liking”) is preserved (4). However, many aspects of the natural history of such dysfunction—that is, whether it is a cause or a consequence of starvation—remain elusive.

Neuroimaging provides a window for objectively evaluating mechanisms of reward processing in anorexia nervosa and may shed light on these open questions. Additionally, it can be used to study similarities with and differences from related conditions, such as bulimia nervosa, helping in the development of biomarkers that can guide future efforts toward disease categorization. A commonly used neuroimaging paradigm in eating disorders involves the evaluation of brain reward pathways when individuals taste a pleasant food (usually sugar). Previous research with this method has identified the engagement of two brain systems: ventral and dorsal (2). The ventral system includes regions such as the amygdala, the anterior insula, ventromedial sectors of the prefrontal cortex, and the ventral striatum. The dorsal system comprises the dorsolateral prefrontal cortex, the parietal cortex, and the dorsal striatum. The interplay between rapid, automatic evaluations generated in the ventral system and top-down cognitive influences arising from the dorsal system results in adaptive guidance of eating behavior on the basis of goals.

In this issue of the *Journal*, Frank et al. (5) provide new insights into the nature of reward dysfunction in eating disorders using voxel-based morphometry (VBM), a technique for automatic computational neuroanatomy. The authors examined differences in brain structure in three groups: patients who were currently ill or recovered from anorexia nervosa; patients with bulimia nervosa; and healthy comparison women. The use of three groups allowed an elegant identification of

overlapping as opposed to disorder-specific brain changes. Compared with healthy subjects, all patients had larger gray matter volume in an area of the ventral system, the gyrus rectus/medial orbitofrontal cortex. Gray matter volume in this region correlated with pleasantness ratings (“liking”) during a sucrose taste perception test prior to scanning. More specifically, the anorexia nervosa groups had increased gray matter volume of the anterior insula in the right hemisphere; in bulimia nervosa patients, a similar effect was observed on the left side. Additionally, gray matter volume in the dorsal striatum was associated with a measure of reward sensitivity (“wanting”), and the groups of recovered anorexia nervosa and bulimia nervosa patients had reduced gray matter volume in this area.

Compared with functional MRI (fMRI), the use of structural neuroimaging techniques such as VBM eliminates the dependence on performance of a functional task inside the MRI scanner and provides anatomical information that is potentially more stable and more closely related to disease traits. Gray matter volume can change for many reasons. Increases or decreases can reflect developmental changes or the effects of use and disuse of a brain structure. The implication of this study is that gray matter volume is related to the amount of mental processing devoted to the task of that brain region. The combination of VBM with taste- and reward-related measures in this investigation corroborated the specificity of the findings and is a major strength of the study. Previous research with structural

neuroimaging in anorexia and bulimia nervosa has shown poor consistency of results across studies (6). The investigation by Frank et al. represents a significant contribution to the field, providing a different picture from the existing data, which suggest regional reductions rather than increases in gray matter volume in anorexia nervosa. Notably, it is the

largest neuroanatomical study in eating disorders to date, and it includes key methodological improvements. To overcome the sensitivity of VBM to hydration status (7), Frank et al. strictly controlled food and fluid intake in the participants with anorexia and bulimia nervosa for 7–10 days before scanning sessions, as part of inpatient or partial hospital treatment. In addition, the authors used the most robust methodology for VBM analysis, with an algorithm to improve image registration (diffeomorphic anatomical registration through exponentiated Lie algebra—DARTEL) (8). They also controlled for the effect of a number of confounding variables, such as medication use. Altogether, the study adhered to high methodological standards that support the validity of the findings.

The study points to the gyrus rectus/medial orbitofrontal cortex as a neural substrate common to anorexia and bulimia nervosa, and potentially a transdiagnostic correlate of eating disorders. In the case of bulimia nervosa, only ill individuals were studied; an additional recovered bulimia nervosa group is necessary to confirm this as a trait in the condition. The gyrus rectus/medial orbitofrontal cortex is predominantly involved in the processing of pleasant stimuli (9). As the authors suggest, this opens the possibility that brain changes determining an elevated capacity to experience pleasure from food (liking the taste) could represent neurodevelopmental contributors to eating disorders and act as an initial trigger of compensatory behaviors (such as decreased wanting for food rewards) early on in the

The study points to the gyrus rectus/medial orbitofrontal cortex as a neural substrate common to anorexia and bulimia nervosa, and potentially a transdiagnostic correlate of eating disorders.

natural history. While this possibility is certainly interesting and aligns well with conceptualizations of reward in eating disorders and previous fMRI data (10), it calls for studies to replicate and elaborate on these findings. Because the investigation did not include vulnerable individuals at a premorbid stage, it is difficult to draw a firm conclusion that the identified changes are primary drivers rather than a consequence of prolonged starvation. It will be important to address this issue in future studies, especially with the use of longitudinal designs.

Disorder-specific changes were identified in the anterior insula, a region involved in sensing and modulating the physiological state of the body (11) and a central node in the taste-reward ventral system (2). A growing body of data supports a link between disturbed processing of interoceptive awareness in this region and the pathophysiology of eating disorders. Indeed, in another fMRI study that appears in this issue, Oberndorfer et al. (12) report differences in anterior insula activation in response to sucrose taste in a group of individuals recovered from anorexia and bulimia nervosa. The study by Frank et al. also found changes in the volume of white matter pathways associated with the insula. These and previous findings pave the way for efforts to develop interventions to modify the activity of this region in eating disorders.

The Frank et al. study provides a significant step toward a better understanding of the neuroanatomy of eating disorders and its association with reward. It is a good example of how structural neuroimaging can inform theories of reward dysfunction in eating disorders and provide insights into their natural history to eventually guide brain-based classifications. We may be years away from being able to use a quick brain scan for reliable single-subject diagnosis, making the identification of eating disorders just “a matter of taste,” but studies like those by Frank et al. and Oberndorfer et al. give us hope that the neuroimaging of eating disorders is moving forward and making significant progress.

References

1. Connan F, Campbell IC, Katzman M, Lightman SL, Treasure J: A neurodevelopmental model for anorexia nervosa. *Physiol Behav* 2003; 79:13–24
2. Kaye WH, Fudge JL, Paulus M: New insights into symptoms and neurocircuit function of anorexia nervosa. *Nat Rev Neurosci* 2009; 10:573–584
3. Keating C, Tilbrook AJ, Rossell SL, Enticott PG, Fitzgerald PB: Reward processing in anorexia nervosa. *Neuropsychologia* 2012; 50:567–575
4. Berridge KC: “Liking” and “wanting” food rewards: brain substrates and roles in eating disorders. *Physiol Behav* 2009; 97:537–550
5. Frank GK, Shott ME, Hagman JO, Mittal VA: Alterations in brain structures related to taste reward circuitry in ill and recovered anorexia nervosa and in bulimia nervosa. *Am J Psychiatry* 2013; 170:1152–1160
6. Van den Eynde F, Suda M, Broadbent H, Guillaume S, Van den Eynde M, Steiger H, Israel M, Berlim M, Giampietro V, Simmons A, Treasure J, Campbell I, Schmidt U: Structural magnetic resonance imaging in eating disorders: a systematic review of voxel-based morphometry studies. *Eur Eat Disord Rev* 2012; 20: 94–105
7. Streitbürger DP, Möller HE, Tittgemeyer M, Hund-Georgiadis M, Schroeter ML, Mueller K: Investigating structural brain changes of dehydration using voxel-based morphometry. *PLoS ONE* 2012; 7:e44195
8. Ashburner J: A fast diffeomorphic image registration algorithm. *Neuroimage* 2007; 38:95–113
9. Grabenhorst F, Rolls ET: Value, pleasure, and choice in the ventral prefrontal cortex. *Trends Cogn Sci* 2011; 15:56–67
10. Uher R, Murphy T, Brammer MJ, Dalgleish T, Phillips ML, Ng VW, Andrew CM, Williams SC, Campbell IC, Treasure J: Medial prefrontal cortex activity associated with symptom provocation in eating disorders. *Am J Psychiatry* 2004; 161:1238–1246
11. Craig AD: How do you feel? Interoception: the sense of the physiological condition of the body. *Nat Rev Neurosci* 2002; 3:655–666
12. Oberndorfer TA, Frank GKW, Simmons AN, Wagner A, McCurdy D, Fudge JL, Yang TT, Paulus MP, Kaye WH: Altered insula response to sweet taste processing after recovery from anorexia and bulimia nervosa. *Am J Psychiatry* 2013; 170:1143–1151

MIGUEL ALONSO-ALONSO, M.D.

From the Berenson-Allen Center for Noninvasive Brain Stimulation, Division of Cognitive Neurology, and the Center for the Study of Nutrition Medicine, Department of Surgery, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston. Address correspondence to Dr. Alonso-Alonso (malonso@bidmc.harvard.edu). Editorial accepted for publication July 2013 (doi: 10.1176/appi.ajp.2013.13070932).

The author is a recipient of research grants from the Boston Nutrition and Obesity Research Center (project 5P30DK046200), the Nutrition Obesity Research Center at Harvard (project P30 DK040561), and Ajinomoto and serves as a scientific adviser for International Life Sciences Institute North America and Wrigley Science Institute; he is also the recipient of a gift from the Rippe Lifestyle Institute. Dr. Freedman has reviewed this editorial and found no evidence of influence from these relationships.