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Anorexia nervosa, neuroimaging research, and the contextual salience of food cues: The food approach–avoidance conundrum

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Abstract

Anorexia nervosa (AN) is characterized by an avoidance and marked apprehension around food intake, yet paradoxically, those with AN often display approach behaviors to food, engaging in food shopping or preparation activities which are described as rewarding. This approach–avoidance conundrum is of much importance as neuroimaging studies continue to probe mechanisms relating to core AN psychopathology. This Idea Worth Researching discusses the notion that neuroimaging studies relying on food cue presentation paradigms may be methodologically flawed without specifying the contextual salience of the food cues presented in paradigms. The appraisal of food cues may diverge as a function of one's intent-to-eat, and thus, neuroimaging studies not specifying the contextual salience of food cues (i.e., intent-to-eat or not) may confound two distinctly different processes.

Keywords

anorexia nervosa; food approach; food avoidance; neuroimaging

1 | INTRODUCTION

Anorexia nervosa (AN) is among the most pernicious of psychiatric disorders, for which the precise pathophysiology remains elusive. While an increasing focus on the mechanisms underpinning AN psychopathology has emerged over the last decade, this has not yet yielded demonstrable advances in treatment outcomes, and the mechanistic processes underlying many symptoms remain incompletely understood. A particularly central and puzzling symptom of AN relates to the complex relationship of those affected with food. Those with AN typically avoid or limit food intake, and periodically endure it with marked

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apprehension and anxiety. In allaying this anxiety, fastidious screening of the caloric content of foods is frequently observed, alongside a rigid and purposeful avoidance of the consumption of the most calorie-rich foods. At the same time, however, those with AN also display approach behaviors to food, and may report sporadic engagement in episodes of subjective overeating (i.e., anorexia nervosa-binge/purge subtype). Moreover, an 'obsessional' interest in food is often observed in those with AN, which may extend to reading cookbooks, collecting food recipes, and even preparing food for others (Beumont, 2002; Bruch, 1978; Friederich & Herzog, 2011; Goldberg et al., 1979; Halmi, 1978). Interestingly, these behaviors are often described as rewarding by those engaging in them.

In the context of this food approach–avoidance conundrum in those with AN, several meaningful questions are apparent. For instance, what are the factors implicated in these divergent responses to food cues in those with AN? How have the mechanisms underpinning these divergent responses been delineated in research efforts aiming to advance our understanding of the pathophysiology of AN? These are important questions as we attempt to advance our understanding of the psychopathology of AN, and ultimately advance treatment outcomes.

In keeping with efforts in broader psychiatric research, recent attempts to identify the specific mechanisms underpinning AN psychopathology have increasingly leveraged neuroimaging technology, which allows for near real-time observation of brain activity. Typically, imaging studies probing the mechanisms of food-related processes in AN have exposed those with AN to a variety of food cues (i.e., highly palatable foods, high calorie foods, large portions of food, etc.), and observed the neural responses to these cues. However, an important consideration, which may have been under-accounted for in light of the potential scope for differential responses (i.e., approach or avoid) to food cues among those with AN, is one's *intent* to eat. That is, those with AN may experience the preparation of palatable food for others as hedonic and rewarding, yet at the same time experience the potential consumption of those very same foods as aversive and anxiogenic. Indeed, emerging evidence points towards divergent responses to food cues in those with AN, purely as a function of intent to eat (Kissileff et al., 2016; Milos et al., 2013). We contest that this important nuance must be a critical consideration in the design and interpretation of neuroimaging studies intended to interrogate the mechanisms underpinning food-related behavior in AN. Without clearly specifying the context in which food cues are presented (i.e., intent to eat or not), it is possible that studies may conflate these potentially discrepant processes.

Context and perceived intentionality are crucial in shaping the interpretation and valence of an array of potentially aversive stimuli. For instance, a standardized aversive cue, delivered in a standardized context, but with diverging inferences surrounding intentionality, may result in markedly different valence ratings and subjective responses (Liljeholm, Dunne, & O'Doherty, 2014). From a neurobiological lens, the determination of intentionality is a highly complex process that implicates several distinct brain regions, although evidence suggests that the mid-anterior insula, a region known to function abnormally in AN (Kaye, Fudge & Paulus, 2009), plays a pivotal role in perceived intentionality (Craig, 2015; Liljeholm et al., 2014; Lewis, Birch, Hall, & Dunbar, 2017). Importantly, the mid-anterior insula projects both to the ventral striatum, which modulates reward seeking and approach behaviors, and to the amygdala, which modulates the detection and of threat and avoidance behaviors (Craig, 2015). These three regions comprise a corticoamygdala–striatal circuit that is centrally implicated in the integration of information relating to salient stimuli, which is critical in the formation of emotionally-informed behavioral responses (Cho, Ernst & Fudge, 2013). Thus, in the context of food cues in those with AN, potentially discrepant valence ratings, determined by insula-driven inferences surrounding the intentionality of the cue, may create the scope for a broad array of neuroimaging findings that conflate approach and avoidance processes, even when presenting standardized cues in standardized contexts.

2 | MIXED RESEARCH FINDINGS

Reflecting this, a multitude of mixed results have emerged from efforts to identify the mechanistic underpinnings of food consumptive behaviors in AN. For instance, some studies of those with AN have found *reduced* psychophysiological reactivity to palatable food images (Soussignan, Jiang, Rigaud, Royet, & Schaal, 2010), and *lesser* attentional allocation to food cues (Giel et al., 2011). Conversely, other studies examining electrocortical responses illustrated a distinct attentional bias *towards* food cues among those with AN, regardless of caloric value (Blechert, Feige, Joos, Zeeck, & Tuschen-Caffier, 2011). Similarly with respect to valence ratings, different studies have suggested both (a) *reduced* pleasure ratings of food images among those with AN (Soussignan et al., 2010), and (b) *comparable* pleasantness ratings of food images (including high-caloric food) between those with AN and controls (Oberndorfer et al., 2013).

Similarly, neuroimaging studies probing the neural response to food cue presentation paradigms have yielded paradoxical responses in both fear- and reward-related circuitry in AN. While some studies suggest *hypoactive* mesolimbic reward circuitry that is downwardly modulated by greater activation of dorsal cognitive control circuitry in response to food cues (O'Hara, Campbell, & Schmidt, 2015), other studies report *greater* activation of reward-related circuitry in those with AN in response to palatable (and highly caloric) food cues (Cowdrey, Park, Harmer, & McCabe, 2011). In keeping, several studies report *hyperactivity* of the amygdala in response to food cues (Joos et al., 2011), whereas others have reported *hypoactivity* of the amygdala in response to food cues (Holsen et al., 2012).

3 | AN IMPORTANT IDEA WORTH RESEARCHING

In light of these paradoxical findings, an important question relates to the potential scope for discrepant inferences around intentionality, and whether the cues used in food presentation paradigms are uniformly situated in a context that is salient (i.e., intention-to-eat) to the psychopathology of AN. Approach behaviors to food, and the avoidance of *eating* food, are distinct processes that may be differentially modulated within key regions involved in the psychopathology of AN. For instance, approach behaviors are typically underpinned by reward anticipation/processing within striatal pathways (Ikemoto & Panksepp, 1999), whereas avoidance behaviors are underpinned by the detection of potential threat or harm within the amygdala and extended amygdala (Davis, Walker, Miles, & Grillon, 2010). However, avoidant behaviors can also be encoded in striatal regions, and may be 'rewarding' in the sense that they facilitate the relief/avoidance of harm, depending on the context in which the cue is presented (Seymour et al., 2005). For instance, the receipt of aversive cues themselves may in fact be 'rewarding', converging in the ventral striatum, if replacing a *more* aversive cue (Seymour et al., 2005). In those with AN, exposure to palatable foods without an explicit intention to eat may represent no threat, or a relief from the potential threat of eating these foods, thus allowing striatum-driven hedonic responding, whereas an explicit intention to eat these same foods introduces a distinct threat which likely drives aversive responding.

A precise understanding of the brain-based mechanisms that underpin both food approach and food avoidance behaviors in AN is crucial to unraveling the neurobiology of AN. To do this, however, neuroimaging food cue presentation paradigms ought to be consistently situated in the context most salient to the psychopathology of AN, which centrally relates to the consumption of foods, rather than the passive observation of food cues. In enhancing the salience of tasks used during fMRI, broader neuroimaging studies typically utilize 'incentive compatible' tasks which require participants to make decisions that influence the outcomes of the task, and therefore involves real-world implications, while neural responses are observed in fMRI. In those with AN, incentive compatible tasks have been used in studies relating to constructs such as cognitive inhibition and reward processing (i.e., monetary tasks after which the participant receives a monetary reward linked to their performance), although fewer studies have used incentive compatible tasks when probing food-related mechanisms. Clearly, incentive compatible tasks with clear real-world and food-related implications are required in obtaining a contextually salient representation of mechanisms likely implicated in the psychopathology of AN. As such, future imaging studies ought to examine the neural response to food cues as a function of their contextual salience, by for instance, instructing participants prior to scanning that the food images displayed will form part of their prescribed meal plan, or alternately, that the foods displayed will not be part of their prescribed meal plan. Moreover, even the interrogation of broader cognitive mechanisms implicated in AN may be located in a context more salient to the psychopathology of AN by linking task performance with subsequent eating behaviors (Foerde, Steinglass, Shohamy, & Walsh, 2015). Certainly though, without specifying the context in which food cues are presented to those with AN, it is unclear whether neuroimaging findings reflect important group differences relating to illness mechanisms, or rather, differences in the inferred contextual salience, intentionality, or valence of food cues. The latter would render neuroimaging data less meaningful as they relate to advancing our understanding of the core mechanisms underpinning AN. Consideration of the context in which food cues are provided in imaging studies interrogating food-related processes in AN would allow for greater control over the potentially confounding variable of intention-to-eat, and moreover, would allow for greater between-trial comparison, which is a crucial endeavor in a field characterized by relatively small sample sizes in imaging studies.

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