Food stimulus norming

Prior to conducting the first study using this stimulus set (1), a group of 12 adults participated in a norming study to collect categorization accuracy scores for the images. Participants were asked to categorize each picture into one of four categories, as described in the statistical analyses section of the manuscript (high-fat/high-sweet, low-fat/high-sweet, high-fat/low-sweet, or low-fat/low-sweet). Mean categorization accuracy for this sample was 93.4% (SD = 0.07). Additionally, food and object pictures were nearly equivalent with respect to participants' naming accuracy (mean food naming accuracy = 99.1% [SD = 0.04], mean non-food naming accuracy = 99.6% [SD = 0.02], $p > .38$) and ratings of how typical each picture was of the food or object depicted (i.e., banana, stapler, etc.) as rated on a 1-7 scale, with higher ratings indicating the picture was extremely typical of the food or object depicted (mean food typicality = 5.09 [SD = 0.68], mean non-food typicality = 5.09 [SD = 0.86], $p > 0.94$).

Supplemental Analyses

Main effects

Two between-groups t-tests were conducted using AFNI's 3dttest++ to examine the main effect of group (anorexia nervosa [AN] versus healthy control [HC]) for response to all food pictures (versus object pictures) and the response to pictures of high palatability foods (versus low palatability foods). The posterior putamen (x=-24, y=-8, z=+13; 172 mm^3; peak t=-3.82; Cohen's d=-1.18) was the only region exhibiting a group difference in response to all food pictures, with AN participants exhibiting a decreased response in this region compared to HC participants. The VTA (x=+4, y=-20, z=-14; 59 mm^3; peak t=-3.46; Cohen's d=-1.10) exhibited a significant main effect of group for the comparison of high palatability foods to low palatability foods.

Body mass index and anxiety

Statistically significant differences between body mass index (BMI) and anxiety (as measured by the state anxiety subscale of the State Trait Anxiety Inventory [2,3]) were found between groups. Higher state anxiety in AN patients was expected, as anxiety is a prominent feature of the disorder. The mean BMI difference between HC and AN participants was 1.5 BMI points, which is a relatively small absolute difference. The statistical significance of this difference was largely driven by the fact that HC females were only included if they had a BMI between 18.5-25, thus restricting the sample's variability and increasing the t-statistic. Nonetheless, because the groups differed on these variables, we conducted analyses to determine if these variables were related to the brain's response to food images in the entire sample. We performed one-sample t-tests using AFNI's 3dttest++ examining the response to all food pictures (with objects as a baseline) and high palatability as compared to low palatability foods, with BMI and anxiety values entered as covariates in separate analyses. Significance testing and regions-of-interest were identical to those utilized in the main analyses of the study.

No significant results were found for BMI or anxiety for the comparison of high versus low palatability foods. Regions exhibiting a significant correlation between BMI or anxiety and response to food pictures are listed in Table S1. The right amygdala is the only region that also had an interaction with visceral sensation ratings. As reported in the main manuscript, this region exhibited a positive relationship with stomach sensation ratings in HC participants and a negative relationship in AN participants.

Table S1. Brain regions exhibiting a relationship between activation in response to food pictures and body mass index or anxiety

Region	Coordinates			Peak *t*	Volume (mm^3)
	x	y	z		
BMI					
L sgACC	-10	-13	-12	3.54	118
STAI - State Anxiety					
R amygdala	+24	-1	-17	-4.19	220
L putamen	-24	-8	+11	-3.67	161
L putamen	-29	+3	+7	-3.72	129

BMI=body mass index; STAI=State-Trait Anxiety Inventory

Comorbidities

Eleven AN participants were diagnosed with at least one comorbid psychiatric disorder. Although our sample size was not sufficient to test for differences between those with and without a comorbid disorder, we visually inspected the graphs of the significant findings reported in our manuscript to determine if the results were driven by comorbid disorders and/or if individuals with comorbid disorders constituted a separate group. We have reproduced the figures from the manuscript displaying the interaction effects between group and visceral sensation ratings in response to food images below, with the scatterplots only exhibiting data points for AN participants, color-coded for comorbidity (see Figures S1 and S2). As is illustrated by these figures, comorbidities did not appear to have a driving effect on the results, nor did individuals with comorbidities constitute a distinct subset of patients.

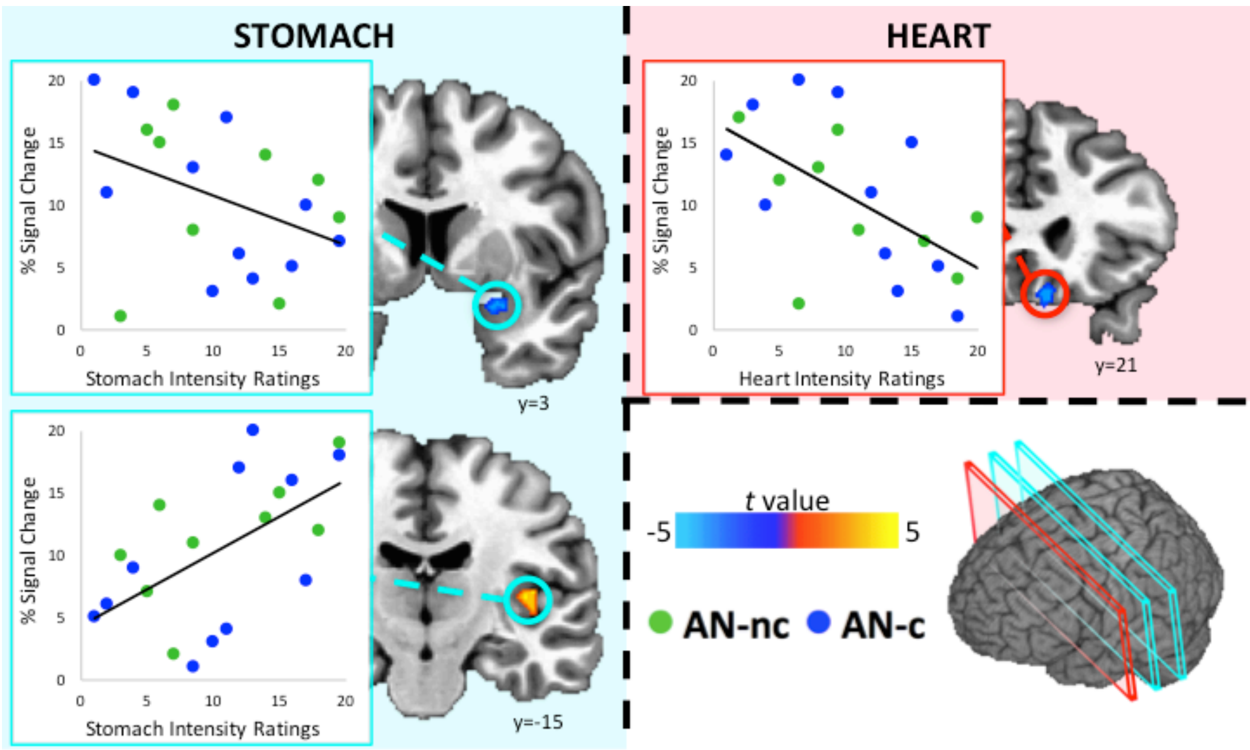

Figure S1. Relationship between interoceptive sensation ratings and activation in response to images of food compared to non-food objects, by comorbid diagnosis. Figure reproduced from Figure 2 (see main article), with healthy control participant data removed from scatterplots for clarity. Data from participants diagnosed with anorexia nervosa are color-coded based on the presence of comorbid diagnoses (green, AN-nc = no comorbid diagnosis; blue, AN-c = presence of a comorbid diagnosis).

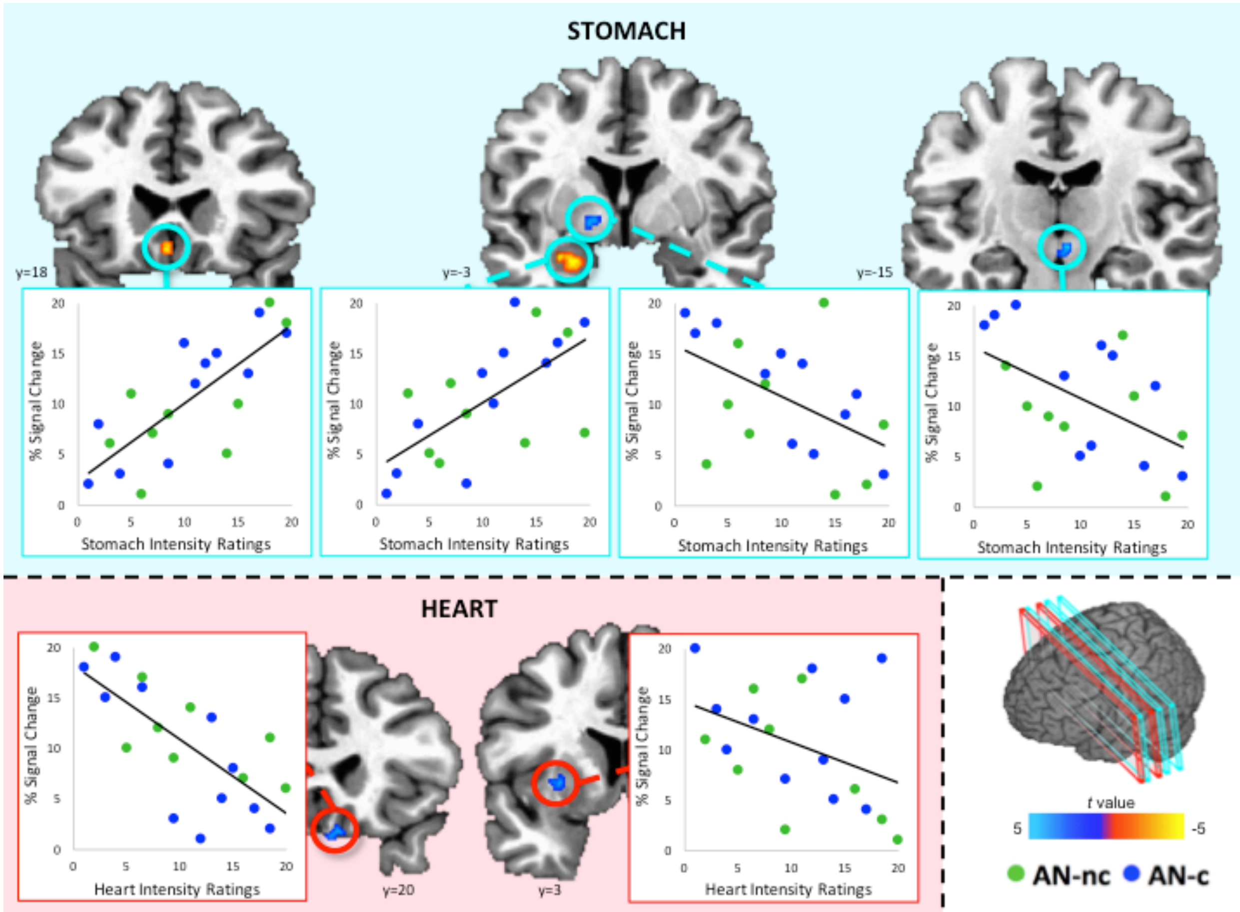

Figure S2. Relationship between interoceptive sensation ratings and activation in response to high palatability food images compared to low palatability food images, by comorbid diagnosis. Figure reproduced from Figure 3 (see main article), with healthy control participant data removed from scatterplots for clarity. Data from participants diagnosed with anorexia nervosa are color-coded based on the presence of comorbid diagnoses (green, AN-nc = no comorbid diagnosis; blue, AN-c = presence of a comorbid diagnosis).

Visceral Sensation Ratings

Table S2 displays group averages for participants' ratings of sensations from the heart, stomach, and bladder during the interoceptive attention task. Please note that these ratings are raw values; for the neuroimaging analyses described in the manuscript, ratings were ranked within each group in order to make the analyses robust to outliers and non-normality.

Table S2. Interoceptive sensation ratings

	AN	HC	*t*	*p*
Stomach	4.47 ± 1.38	3.32 ± 1.35	2.67	0.011
Heart	3.77 ± 1.09	2.59 ± 1.20	3.25	0.002
Bladder	3.92 ± 0.99	2.68 ± 1.61	2.92	0.006

AN=anorexia nervosa; HC=healthy control
Values represent raw data and were rank transformed prior to neuroimaging analyses.

References

(1) Simmons WK, Rapuano KM, Kallman SJ, Ingeholm JE, Miller B, Gotts SJ, Avery JA, Hall KD, Martin A. Category-specific integration of homeostatic signals in caudal but not rostral human insula. Nat Neurosci 2013;16:1551–2.

(2) Spielberger CD, Gorsuch RL, Lushene RE. Manual for the State-Trait Anxiety Inventory, Consulting Psychologists Press, Palo Alto, CA, 1970.

(3) Spielberger CD. State-Trait Anxiety Inventory for Children, Consulting Psychologists Press, Palo Alto, CA, 1973.