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Increased Functional Connectivity Between Ventral Attention and Default Mode Networks in Adolescents with Bulimia Nervosa

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Abstract

Objective: Bulimia nervosa (BN) is characterized by excessive attention to self and, specifically, body shape and weight, but the ventral attention (VAN) and default mode networks (DMN) that support attentional and self-referential processes are understudied in BN. We assessed whether altered functional connectivity within and between these networks contributes to such excessive concerns in adolescents with BN, early the course of the disorder.

Method: Resting-state functional magnetic resonance imaging scans were acquired from 33 BN and 37 healthy comparison (HC) adolescents (aged 12 to 21 years), group-matched by age and body mass index. Region-of-interest analyses were performed to examine group differences in

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functional connectivity within and between the VAN and DMN. We further explored associations of VAN-DMN connectivity with BN symptoms, body shape/weight concerns, and sustained attention on the Continuous Performance Test (CPT).

Results: Compared to HC adolescents, those with BN showed significantly increased positive connectivity between right ventral supramarginal gyrus and all DMN regions, as well as between right ventrolateral prefrontal cortex and left lateral parietal cortex. Within-network connectivity did not differ between groups. VAN-DMN connectivity was associated with BN severity and body shape/weight concerns in the BN group. No significant group-by-CPT interactions on VAN-DMN connectivity were detected.

Conclusion: Increased positive VAN-DMN connectivity in adolescents with BN may reflect abnormal engagement of VAN-mediated attentional processes at rest, perhaps related to their excessive attention to self-referential thoughts about body shape/weight. Future studies should further investigate these circuits as targets for the development of early interventions aimed at decreasing excessive body shape/weight concerns.

Keywords

Bulimia Nervosa; Adolescence; Functional Magnetic Resonance Imaging

INTRODUCTION

Bulimia nervosa (BN) is an intractable eating disorder that typically emerges during adolescence and is characterized, in part, by excessive concern with and selective attention to body shape and weight (shape/weight). Such negative self-referential thoughts contribute to the maladaptive pattern of food restriction, binge eating, and purging that defines BN.¹ Behavioral data suggest that BN pathology is indeed associated with excessive attention to self- and shape/weight-related stimuli, but the neural networks that support attentional and self-referential processes in BN are understudied.^{2,3} Identifying disruptions in the function and connectivity of these circuits, particularly in adolescents with BN, may foster the development of early interventions that target these circuits to reduce excessive shape/weight concerns that likely contribute to the persistence of BN into adulthood.

Body image disturbance is central to BN, and flawed cognitions about shape/weight, coupled with societal pressures for thinness, lead individuals with BN to preferentially attend to negative aspects of their own bodies.^{4,5} Prioritizing such negative cognitions may reinforce negative body image in BN, perpetuating bingeing and purging behaviors.^{6,7} Behavioral findings point to selective attention to shape/weight-related words and images in BN individuals,^{8–10} and suggest an association between self-referential thoughts and attention bias to shape/weight-related stimuli.^{11,12} Individuals with BN are continuously exposed to environmental cues (i.e. internal and external shape/weight stimuli) that invoke anxiety, provoke negative cognitions, and perpetuate their destructive behaviors.¹³ Weight-related and body image concerns persist even after long-term symptomatic recovery from BN.¹⁴ Probing the neural circuits that underlie self-referential thoughts and selective attention to shape/weight stimuli in BN may improve our understanding of BN

pathophysiology and foster research into circuit-based treatments for altered cognitions in BN.

Attentional and self-referential processes are supported, in part, by intact functioning of task-positive and task-negative networks at rest and in response to task demands.¹⁵ The ventral attention network (VAN) is a task-positive network that supports the identification of salient or novel environmental stimuli and is typically activated during attentional orientation or reorientation.^{16,17} It is a right-lateralized network of regions including ventrolateral prefrontal cortex (VLPFC) and the temporo-parietal junction (TPJ), subdivided into right posterior superior temporal gyrus (pSTG) and ventral supramarginal gyrus (rvSMG).^{18,19} Conversely, the default mode network (DMN) is a task-negative network activated in response to stimulus-independent, self-referential and emotional thoughts.²⁰ The DMN is comprised of the posterior cingulate (PCC), precuneus, medial prefrontal (MPFC), and left/right lateral parietal cortices (LLP/RLP).²⁰ In healthy individuals, activation in these networks is typically negatively correlated (i.e. anticorrelated) during attention-demanding tasks and at rest.^{21,22} Anticorrelated activity across task-positive and task-negative networks promotes elasticity in attentional allocation between intrinsic and extrinsic environmental stimuli and is associated with healthy neural development.^{15,23}

The neural correlates of attention to body-related stimuli in BN have been assessed in task-based fMRI studies showing altered functioning of regions involved in self-referential processing.^{24–28} However, findings vary depending on the stimuli presented (i.e., human or non-naturalistic bodies) and comparison groups studied (i.e., healthy individuals or those with Anorexia Nervosa [AN]). Specifically, BN compared to healthy women show reduced activation of DMN regions (PCC/precuneus^{24,25} and MPFC²⁸) when comparing their bodies to others' or rating distorted self-images, but increased activation of these regions when imagining someone comparing their bodies to a 'fat' computer-generated body.²⁷ Although inconsistent, these findings suggest disrupted DMN functioning in BN individuals, perhaps contributing to their excessive attention to shape/weight.

To our knowledge, only one previous study assessed the functioning of attention networks in adolescents and young adults with BN in the absence of disorder-relevant stimuli.²⁹ Compared to healthy youth, those with BN failed to deactivate the precuneus (DMN region) or appropriately activate the TPJ (VAN region) when alerting and reorienting to cues on an attention network task.²⁹ These findings suggested that youth with BN are unable to navigate away from their internal preoccupation with self (i.e., shape/weight concerns), contributing to their DMN activation rather than deactivation when attending to task stimuli. Similar patterns of DMN activation (i.e. reduced task suppression) in adults with major depressive disorder (MDD) when processing emotional stimuli^{30,31} further suggest that DMN-mediated self-focused rumination may interfere with task-positive attention network function, thereby contributing to attentional deficits.³² Thus, altered DMN functioning may be associated with negative rumination transdiagnostically, and altered processing within both DMN and VAN may be associated with abnormal or excessive attention to shape/weight in BN.

Resting-state fMRI (R-fMRI) measures spontaneous blood-oxygen-level dependent (BOLD) signal fluctuations among brain regions in the absence of task stimuli.^{20,33} R-fMRI reflects intrinsic interactions between functionally connected (i.e. temporally correlated) brain regions-of-interest (ROIs), and thus allows investigation of functional brain organization unconfounded by task type or stimulus. Previous R-fMRI studies assessed cerebellar,³⁴ somatosensory,³⁵ anterior insular,³⁶ interhemispheric,³⁷ and whole-brain³⁸ connectivity in adults with BN. Only one study assessed connectivity across task-positive and task-negative network regions in adults with BN, showing positive connectivity in BN (compared to negative connectivity in healthy participants) that was associated with greater body shape concerns.³⁹ Unknown is whether this altered pattern of connectivity contributes to shape/weight concerns or arises as a result of, such distorted cognitions. Studying connectivity across these circuits in adolescence will contribute to our understanding of their function early in the course of BN, and serve as a first step towards preventing their altered development into adulthood.

Herein, we used R-fMRI to assess within- and between-network connectivity of the VAN and DMN in adolescent females with BN. Previous task-based findings from youth with BN²⁹ and resting-state findings from adults with BN³⁹ suggest disrupted functional connectivity between task-positive and task-negative networks in BN. As such, we hypothesized that VAN-DMN connectivity would be altered in adolescents with BN, with positive connectivity in BN compared to negative connectivity in HC, consistent with findings from adults with BN.³⁹ We also hypothesized that such positive VAN-DMN connectivity would be associated with the frequency of BN symptoms, and specifically, greater shape/weight-related concerns in the BN group, suggesting the intrusion of DMN-mediated self-referential thoughts on VAN-mediated attentional processing. Lastly, to determine whether altered VAN-DMN connectivity contributes to overall attentional deficits in BN, we explored associations of VAN-DMN connectivity with performance on the Continuous Performance Test across groups.

METHOD

Participants

Female adolescents with BN (n= 33) and healthy controls (HC) (n = 37), group-matched for age, body mass index (BMI), race, and ethnicity, were recruited for study participation. Demographic and clinical characteristics of the samples are displayed in Table 1. Formal BN and comorbid psychiatric diagnoses in all participants were made using the Structured Clinical Interview for DSM Disorders⁴⁰ for adolescents 18 years and older, and the Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime⁴¹ for those under 18 years. Diagnoses were confirmed via clinical interviews with a psychiatrist. Controls had no current or lifetime DSM 5 diagnoses. Participants with BN and comorbid psychiatric diagnoses (except depression or anxiety) were excluded. Additional inclusion and exclusion criteria are outlined in Supplement 1, available online. BN symptom severity and prior AN diagnoses were assessed using the Eating Disorders Examination (EDE).⁴² Shape and weight concerns were self-reported via the EDE-Questionnaire (EDE-Q).⁴³ Participants with BN were scanned prior to being offered outpatient or inpatient

treatment as part of their study participation. Those taking medications were not excluded, but those taking stimulants were instructed not to take them on the day of their scan. The Institutional Review Board of the New York State Psychiatric Institute approved this study, including all informed consent and assent procedures.

Conners' Continuous Performance Test-II (CPT)

Participants completed the standard computerized CPT on the same day as their MRI scan (see Supplement 1, available online). CPT raw scores were converted to age-adjusted T scores, with higher T scores indicating worse performance.

Image Acquisition and Processing

Image acquisition and processing procedures are detailed in Supplement 1, available online. Two 5-min R-fMRI scans were acquired per participant using a GE Signa 3T Whole-Body Scanner at the New York State Psychiatric Institute. Participants were instructed to lie awake with their eyes closed. T1-weighted sagittal localizing images were acquired, followed by a 3-dimensional (3D) spoiled gradient recall (SPGR) image for coregistration with axial echoplanar images. Whole brain coverage with an effective resolution of $3.75 \times 3.75 \times 3.5$ mm was acquired using axial echoplanar images (TR = 2,200 msec, TE = 25 msec, 90° flip angle, single excitation per image, slice thickness 3.5 mm, 24×24 cm field of view, 64×64 matrix, no skip).

Standard image preprocessing and first-level analyses were applied using SPM12 (<http://www.fil.ion.ucl.ac.uk/spm/>) and the CONN toolbox (detailed in Supplement 1, available online).⁴⁴ The CONN toolbox employs anatomical component-based noise correction method (aCompCor)⁴⁵ rather than average global signal regression (GSR) to reduce the physiological and other sources of noise in BOLD signal.⁴⁶ This method corrects for physiological noise by regressing out signal from WM and CSF that is unrelated to neural activity. Although aCompCor and GSR with 36 parameters are similarly effective in mitigating the effects of motion,⁴⁷ using aCompCor ensures that observed anticorrelations in functional connectivity are not due to artifacts introduced by GSR.⁴⁶

ROI Definition

ROIs for the VAN (VLPFC, pSTG, rvSMG) were defined based on a prior study of this network,¹⁹ and were 10 mm diameter spherical regions centered at peak coordinates (converted to MNI space,⁴⁸ Figure 1A, Table S1, available online). These ROIs were empirically derived from functional networks in adults,¹⁸ but are preserved across development. Analyses exploring the sensitivity and specificity of our VAN ROIs are presented in Table S2, available online. ROIs for the DMN (MPFC, LLP, RLP, and PCC) were defined *a priori* in the CONN toolbox (Figure 1B, Table S1, available online)⁴⁴ and are commonly accepted as major nodes of the DMN.^{20,21}

Behavioral Analyses

Before performing statistical analyses, we examined the distributions of CPT performance data to identify outliers. Group differences in CPT performance were tested using two-sample t-tests with unequal variance.

A Priori Hypothesis Testing

Group Differences in VAN-DMN Connectivity—Functional connectivity analyses to assess for group differences in within- and between-network connectivity were performed using a seed-based ROI to ROI approach implemented in the CONN toolbox.⁴⁴ For each participant, the average BOLD time series for all voxels in each seed ROI was extracted and Fisher-z-transformed. Pairwise Pearson's correlation coefficients were computed between the time courses for each of the ROIs, producing a symmetrical 7 by 7 correlation matrix. The resultant correlation coefficients were compared using two-sample *t*-tests to assess group differences in within- and between-network connectivity. Results were age-adjusted and thresholded based on a false discovery rate (FDR) of $p_{fdr} < .05$. Mean between-network connectivity was calculated by averaging ROI-ROI pairwise correlations across each network, and group differences assessed using two-sample *t*-tests, thresholded at $p < .05$. Pearson's correlations of mean between-network connectivity with age were additionally explored in each group.

Clinical Correlates—Spearman's correlations were performed between within- and between- VAN-DMN pairwise correlations that showed significant group differences and five measures of BN symptom severity, including the frequency of objective (OBEs) and subjective bulimic (SBEs), LOC eating, and vomiting episodes over the past month, as well as shape/weight concerns (combined EDE-Q subscales). Clinical correlates of VAN-DMN connectivities that did not differ across groups were additionally explored (Supplement 1, available online).

Exploratory Analyses

Associations with CPT Performance—Group differences in associations of VAN-DMN connectivity with CPT measures were assessed by testing the significance of group-by-CPT interactions on connectivity, while controlling for IQ. Non-significant interactions were eliminated.

Potential Confounding Effects—Group differences in VAN-DMN connectivity were additionally assessed after excluding those participants with BN who were taking psychotropic medications ($n = 7$), those with comorbid MDD ($n = 9$), comorbid anxiety ($n = 3$), or a lifetime history of AN ($n = 5$).

RESULTS

Participants

R-fMRI scans were acquired from 33 adolescent females with BN (aged 14-21 years) and 37 age- and BMI-matched HC adolescents (aged 12-21 years) (Table 1). The groups did not differ significantly on age, BMI, or IQ. All participants with BN met DSM 5 criteria for BN. Seven participants with BN additionally met DSM 5 criteria for MDD, one for generalized anxiety disorder, one for social anxiety disorder, one for MDD and dysthymia, and one for MDD and specific phobia. Seven participants with BN were on psychotropics, including selective serotonin reuptake inhibitors (SSRI) ($n = 3$), selective norepinephrine reuptake

inhibitor ($n = 1$), stimulants ($n = 1$), antipsychotic ($n = 1$), and both an SSRI and stimulant ($n = 1$).

Behavioral Performance

BN compared to HC participants made more commission errors ($p = .002$) and had higher detectability ($p = .001$) scores on the CPT, but CPT performance was unassociated with BN symptoms in the BN group ($ps = .05$).

A Priori Hypothesis Testing

Group Differences in VAN-DMN Connectivity—Relative to HC participants, those with BN showed significantly greater VAN-DMN connectivity. Positive connectivity was detected in the BN group between rvSMG and all DMN regions: rvSMG-MPFC ($p_{\text{fdr}} < .021$), rvSMG-LLP ($p_{\text{fdr}} < .001$), rvSMG-RLP ($p_{\text{fdr}} < 0.007$), and rvSMG-PCC ($p_{\text{fdr}} < .001$; Table 2, Figure 2). Positive connectivity was additionally detected between VLPFC and LLP ($p_{\text{fdr}} < .036$; Table 2, Figure 2). Positive mean VAN-DMN connectivity was detected in BN compared to healthy adolescents ($p = .003$). In contrast, neither positive nor negative mean VAN-DMN connectivity was detected in the HC group ($ps > .05$, Figure S1, available online). Within-network connectivity did not differ across groups ($p_{\text{fdr}} > .05$), and age was uncorrelated with mean VAN-DMN connectivity in either group (Figure S2, available online). See Supplement 1, available online, for within- and between-network correlation matrices (Figure S1, available online).

Clinical Correlates—In the BN group, positive VAN-DMN connectivity was associated with more frequent BN symptoms and greater shape/weight concerns. Specifically, rvSMG-RLP connectivity positively associated with the frequency of OBEs ($p = .005$, uncorrected), LOC ($p = .007$, uncorrected) and vomiting episodes ($p = .029$, uncorrected) over the past month (Figure 3, Table S3, available online). RvSMG-LLP and VLPFC-LLP connectivity positively associated with shape/weight concerns on the EDE-Q subscales ($ps = .05$, uncorrected; Figure 3, Table S3, available online). Mean VAN-DMN connectivity also correlated positively with shape/weight concerns ($p = .04$, uncorrected; see Table S3, available online).

Exploratory Analyses

Associations with CPT Performance—Significant group-by-CPT interactions on VAN-DMN connectivity were not detected, but rvSMG-LLP and rvSMG-RLP connectivity positively associated with commission errors and detectability scores across all participants ($ps < .01$).

Potential Confounding Effects—Excluding participants with BN on medications, with comorbid MDD or anxiety, or a lifetime history of AN revealed similarly increased positive VAN-DMN connectivity (see Table S4, available online). Increased positive VLPFC-LLP (BN vs. HC) remained and MPFC-RLP connectivity (HC > BN) emerged in the AN- and MDD-excluded groups, respectively (see Table S4, available online). Depressive symptoms (Beck Depression Inventory) were not associated with VAN-DMN (or within-DMN) connectivity in the BN group ($ps > .05$).

DISCUSSION

We investigated functional connectivity across attentional and self-referential circuits in adolescents with BN to identify circuit-based abnormalities that might underlie the development of distorted cognitions about body shape and weight. Increased positive VAN-DMN connectivity was associated with the frequency of their binge-eating and purging behaviors as well as their body shape/weight concerns. Although adolescents with BN performed worse on the CPT, no significant group-by-CPT interactions on VAN-DMN connectivity emerged. Thus, increased positive VAN-DMN connectivity may not contribute to overall attentional deficits in BN, but rather to preferential attention to self-referential thoughts and, specifically, distorted shape/weight cognitions that tend to perpetuate BN behaviors.

The VAN and DMN serve opposing psychological functions and are negatively correlated at rest²¹ and in response to task demands in healthy individuals.¹⁷ BN adolescents showed increased positive functional connectivity between rvSMG (VAN region) and all DMN regions and VLPFC and LLP, respective VAN and DMN regions. Correlations across DMN and attentional networks mirror activity across major hubs of either network,⁴⁹ consistent with our finding of increased positive mean VAN-DMN connectivity in BN compared to healthy adolescents. Although the VAN and DMN were uncorrelated in our modest sample of healthy adolescents and age effects on VAN-DMN connectivity were not detected, cross-sectional data from larger samples of healthy youth (ages 8 – 24 years) suggest that task-positive and task-negative networks are positively correlated during childhood before becoming negatively correlated over late adolescence and into adulthood.^{50–52} Thus, our finding of uncorrelated VAN-DMN connectivity in HC adolescents may reflect the normal pattern of development between task-positive and task-negative networks.

Developmental increases in negative connectivity across task-positive and task-negative networks correspond with improvements in attention and cognitive control processes,⁵³ and stronger negative connectivity has been associated with improved performance and greater cognitive control during task performance in adolescents and adults.^{51,54} In contrast, less negative or positive connectivity between these networks has been observed in other patient populations, including adults with AN,³⁹ OCD,⁵⁵ MDD,³¹ and children with attention-deficit hyperactivity disorder.^{56,57} Positive VAN-DMN connectivity in adolescents with BN is consistent with findings of positive connectivity across task-positive and task-negative networks in adults with the disorder.³⁹ Such altered connectivity across task-positive and task-negative networks may be present early in the course of BN. Unknown is whether positive VAN-DMN connectivity, specifically, or positive connectivity across task-positive and task-negative networks, more broadly, reflects an altered developmental trajectory of these networks in adolescents with BN.

BN adolescents are preoccupied with negative self-referential thoughts of their bodies,⁵⁸ perhaps leading to their preferential attention to related stimuli.^{9,10} Behavioral findings indeed suggest attention bias to shape/weight related stimuli in BN.^{2,12,13} The VAN supports attentional allocation toward novel, behaviorally-relevant stimuli. Conversely, the DMN supports self-referential thought processes, and increased activity has been associated with

excessive focus on negative, self-referential³¹ and body-related²⁷ thoughts. Thus, positive rather than negative VAN-DMN connectivity in BN adolescents may represent excessive rumination about shape/weight that may interfere with the appropriate suppression of task-positive networks at rest. Such interpretation is consistent with our findings that greater VAN-DMN connectivity in BN was associated with more frequent BN symptoms and greater shape/weight concerns, as well as with findings from adults with BN.³⁹ Specifically, this latter study showed that positive connectivity between dorsal anterior cingulate (dACC) – i.e., a hub of task-positive networks (i.e., cingulo-opercular and salience) – and precuneus – i.e., a hub of the DMN⁵⁹ – was associated with greater body shape concerns.³⁹ Thus, self-referential thoughts, specifically shape/weight concerns, may be associated with disrupted connectivity across task-positive and task-negative networks in BN.

Increased VAN-DMN connectivity in BN adolescents may interfere with the engagement of these networks in response to task demands given previous findings of reduced DMN deactivation and VAN activation in BN compared to healthy adolescents during an attentional network task.²⁹ Those findings suggested that a preoccupation with disorder-relevant thoughts may preclude BN adolescents from shifting attention away from those thoughts in response to task demands.²⁹ Task-based and R-fMRI findings from individuals with anxiety disorders indeed suggest that altered activation of VAN regions^{60,61} and altered within-VAN connectivity¹⁹ may underlie attention biases towards threatening stimuli. Intrusion of DMN-mediated, self-critical thoughts may similarly interfere with the suppression of task-positive networks in adolescents with BN. Together, these findings suggest that disturbances in the function and connectivity of the VAN and DMN likely contribute to aspects of BN phenomenology and warrant further investigation.

Adolescents with BN performed worse on the CPT, but performance was unassociated with BN symptoms. Although VAN-DMN connectivity was associated with CPT performance across all participants, significant group-by-CPT interactions on connectivity were not detected. These circuits likely support attentional processes measured by the CPT, but the relationship of VAN-DMN connectivity with CPT performance may not be specific to BN. For example, CPT performance in healthy⁶² and psychiatric⁶³ populations is associated with activation of regions (e.g., temporo-parietal) outside of the VAN, DMN, and other control circuits (e.g., fronto-striatal and fronto-parietal) that may be markers of BN or BN symptoms.^{64,65} Alternatively, the relationship between VAN-DMN and BN symptoms may reflect attentional deficits in BN that are not captured by the CPT, such as attention bias to shape/weight stimuli and concerns.

This study is limited by the modest sample size and inclusion of BN adolescents with comorbid depression and anxiety disorders. Although sensitivity analyses did not reveal a significant effect of these comorbid illnesses on VAN-DMN connectivity, exclusion of comorbid MDD revealed increased MPFC-RLP connectivity in HC vs. BN adolescents. DMN dysfunction has been reported in MDD,³¹ and future studies should evaluate this contribution to functional connectivity in BN. Additionally, since our clinical correlations were not corrected for multiple comparisons, these findings should be interpreted with caution. Although we did not control for time of scanning, there were no group differences in this variable (see Supplement 1, available online). We also did not control for hunger/

satiety or menstrual status. Hunger might affect attentional processes or contribute to increased preoccupation with food during scanning.⁶⁶ Menstrual status may also affect attention-related neural functioning.⁶⁷ Although we have no reason to believe that hunger or menstrual status differed across groups, our findings should be interpreted with caution prior to replication in a larger sample. Finally, we cannot conclude from this cross-sectional study whether increased VAN-DMN connectivity underlies the development of BN (state) or develops as a result of the disorder (trait). Distinguishing between state and trait characteristics in BN is important for informing etiological, prevention, and treatment models.⁶⁸ Future longitudinal studies should assess VAN-DMN connectivity in youth at-risk of developing BN or those with subclinical symptoms to determine whether altered between-network connectivity can predict the development or persistence of BN over adolescence and young adulthood.

In conclusion, our findings suggest that disrupted functional connectivity across the VAN and DMN may contribute to body-related concerns in adolescents with BN. Adolescents with BN demonstrated altered VAN-DMN connectivity, and positive VAN-DMN connectivity was associated with BN symptom frequency and shape/weight concerns. Thus, altered VAN-DMN connectivity in adolescents with BN may reflect DMN-mediated preoccupations with anxiety-provoking, self-referential stimuli that, in turn, may intrude on VAN-mediated attentional processes, even in the absence of attention-demanding tasks. As such, altered VAN-DMN connectivity may, in part, contribute to the attention bias toward shape/weight stimuli that has previously been implicated in the development and persistence of BN.^{2,13} Future studies should determine whether altered VAN-DMN connectivity precedes the onset of BN or arises as a result of the disorder, in hopes that these neuroimaging findings could guide the development of targeted, circuit-level interventions aimed at reducing attention bias and maladaptive binge-eating and purging behaviors.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1. Visual Representation of Ventral Attention (VAN) and Default Mode Network (DMN) Regions-of-Interest (ROIs)

Note: Location of the (A) three VAN and (B) four DMN ROIs used in this study. LLP = left lateral parietal; MPFC = medial prefrontal cortex; PCC = posterior cingulate cortex; pSTG = posterior superior temporal gyrus; RLP = right lateral parietal; ROI =; rvSMG = right ventral supramarginal gyrus; VLPFC = ventrolateral prefrontal cortex

Figure 2. Group Differences in Resting State Functional Connectivity Across Ventral Attention and Default Mode Network (VAN-DMN) Regions

Note: Bar graphs illustrate mean resting state functional connectivity strength between (A) rvSMG and the PCC ($p_{\text{fdr}} < .00$) and (B) VLPFC and LLP ($p_{\text{fdr}} < .04$). BN = bulimia nervosa; HC = healthy control; LLP = left lateral parietal cortex; MPFC = medial prefrontal cortex; PCC = posterior cingulate cortex; pSTG = posterior superior temporal gyrus; RLP = right lateral parietal cortex; rvSMG = right ventral supramarginal gyrus; VLPFC = ventrolateral parietal cortex

Figure 3. Associations of Ventral Attention and Default Mode Network (VAN-DMN) Connectivity with Symptom Severity in Adolescents with Bulimia Nervosa (BN)

Note: Positive associations of rvSMG-RLP connectivity with the frequency of (A) OBEs, (past month, log-transformed, $r = .49$, $p < .004$, uncorrected) and (B) vomiting (past month, log-transformed, $r = .38$, $p < .028$, uncorrected). Positive associations of (C) rvSMG – LLP connectivity with shape/weight concerns ($r = .38$, $p < .044$, uncorrected) and (D) VLPFC – LLP connectivity with shape/weight concerns ($r = .38$, $p < .047$, uncorrected). LLP = left

lateral parietal cortex; OBEs = objective bulimic episodes; RLP = right lateral parietal cortex; rvSMG = right ventral supramarginal gyrus; VLPFC = ventrolateral prefrontal cortex

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Table 1.

Demographic and Clinical Characteristics of Participants

Characteristic	Bulimia Nervosa (n =33)			Healthy Control (n =37)			Analysis	
	Mean (SD)	Median (IQR)		Mean (SD)	Median (IQR)		t	p
Age, y	17.5 (1.6)	18 (3)		16.9 (2.3)	17 (4)		0.19	0.48
Height, in	63.9 (2.9)	64 (4)		64.1 (2.6)	64 (3)		0.79	0.76
Weight, lb	128.4 (17.5)	127 (16)		127.7 (19.6)	125 (17)		0.88	0.76
BMI	22.1 (3.1)	21.6 (3.5)		21.8 (2.6)	21.7 (4.6)			
WASI IQ Score, Full	109.2 (10.1)	110 (11)		109.8 (16.4)	111 (22)		0.85	0.89
BDI ^a	18.8 (10.6)	16.5 (15)		2.1 (2.3)	2 (3)		-0.79	<0.01
EDE Ratings								
OBEs, past 28 days	20.7 (21.4)	15 (22)						
SBEs, past 28 days	19.7 (23)	12 (23)						
LOC eating, past 28 days	37.3 (28.4)	27 (36)						
Vomiting, past 28 days	42.7 (46.7)	27 (37)						
Duration of illness, mo	29.7 (20.7)	24 (24)						
Race/Ethnicity								
White	21	63.6	15		40.5		5.08 (5)	0.41
African American	3	9.1	5		13.5			
Hispanic	4	12.1	8		21.6			
Asian	4	12.1	5		13.5			
Other	0	0	2		5.4			
Did not disclose	1	2.4	2		5.4			
Past AN	5	15.2	-					
Comorbid MDD	9	27.7	-					
Comorbid Anxiety	3	9.1	-					
Medications	7	21.2	-					

Note: AN = anorexia nervosa; BDI = Beck Depression Inventory; BMI = body mass index; EDE = Eating Disorders Examination; LOC = loss of control; MDD = major depressive disorder; OBE = objective bulimic episodes; SBE = subjective bulimic episodes; WASI = Wechsler Abbreviated Scale of Intelligence.

^aBDI scores were collected in n = 28 adolescents with BN and n = 26 healthy controls

Table 2.

Group Differences in VAN-DMN Connectivity

ROI-ROI	Contrast	Peak t	p uncorr.	p FDR-corr.
rvSMG-MPFC	BN > Controls	2.52	0.01	0.02
rvSMG-LLP	BN > Controls	3.77	0.00	0.00
rvSMG-RLP	BN > Controls	3.05	0.00	0.01
rvSMG-PCC	BN > Controls	3.86	0.00	0.00
VLPFC-LLP	BN > Controls	2.84	0.01	0.04

Note: BN = bulimia nervosa; DMN = default mode network; FDR = false discovery rate; rvSMG = right ventral supramarginal gyrus; MPFC = medial prefrontal cortex; LLP = left lateral parietal cortex; RLP = right lateral parietal cortex; PCC = posterior cingulate cortex; VAN = ventral attention network; VLPFC = ventrolateral prefrontal cortex